```
=> b reg
FILE 'REGISTRY' ENTERED AT 08:44:11 ON 20 JUL 2006
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STRUCTURE FILE UPDATES:   18 JUL 2006  HIGHEST RN 894196-03-3
DICTIONARY FILE UPDATES:  18 JUL 2006  HIGHEST RN 894196-03-3

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

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REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d ide can l9 tot

L9   ANSWER 1 OF 3  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   340019-70-7  REGISTRY
ED   Entered STN:  07 Jun 2001
CN   Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-2-
     (methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI)  (CA
     INDEX NAME)
FS   STEREOSEARCH
MF   C24 H28 N2 O6 S
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
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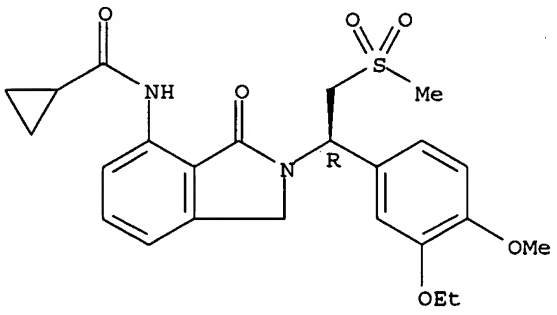


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

               5 REFERENCES IN FILE CA (1907 TO DATE)
               5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE   1:  144:460857

REFERENCE   2:  143:472631

REFERENCE   3:  140:350585
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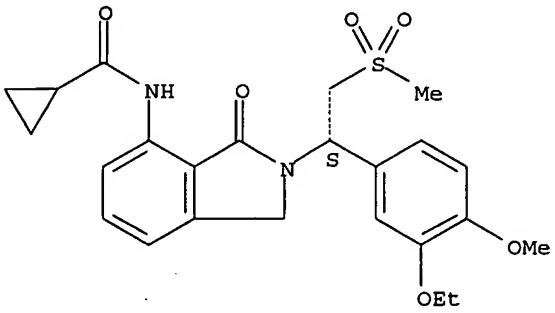
REFERENCE 4: 140:42030

REFERENCE 5: 134:366799

L9 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2006 ACS on STN
RN 340019-69-4 REGISTRY
ED Entered STN: 07 Jun 2001
CN Cyclopropanecarboxamide, N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C24 H28 N2 O6 S**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

6 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 145:55949

REFERENCE 2: 144:460857

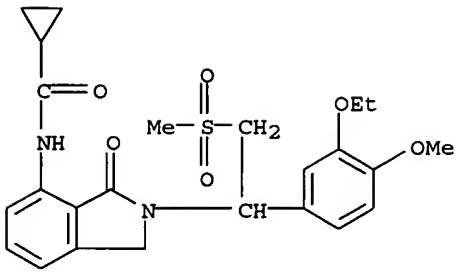
REFERENCE 3: 143:472631

REFERENCE 4: 140:350585

REFERENCE 5: 140:42030

REFERENCE 6: 134:366799

L9 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2006 ACS on STN
RN 340019-67-2 REGISTRY
ED Entered STN: 07 Jun 2001
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF **C24 H28 N2 O6 S**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

18 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
18 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 145:55949

REFERENCE 2: 144:460857

REFERENCE 3: 144:583

REFERENCE 4: 144:582

REFERENCE 5: 143:472631

REFERENCE 6: 143:416245

REFERENCE 7: 142:476229

REFERENCE 8: 142:457121

REFERENCE 9: 141:248733

REFERENCE 10: 140:417943

=> b hcap
FILE 'HCAPLUS' ENTERED AT 08:44:29 ON 20 JUL 2006


FILE COVERS 1907 - 20 Jul 2006 VOL 145 ISS 4
FILE LAST UPDATED: 19 Jul 2006 (20060719/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> d all hitstr l17 tot

L17  ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2006 ACS on STN
AN   2005:1259318  HCAPLUS
DN   144:583
ED   Entered STN:  01 Dec 2005
TI   Methods and compositions using selective cytokine inhibitory drugs for
     treatment and management of cancers and other diseases
IN   Zeldis, Jerome B.
PA   Celgene Corporation, USA
SO   PCT Int. Appl., 89 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  A61K-0031/40
     ICS  A61K-0031/44
CC   1-6 (Pharmacology)
FAN.CNT 1
     PATENT NO.           KIND  DATE        APPLICATION NO.          DATE
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PI   WO2005112918          A1    20051201    2004WO-US14002           20040505
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
PRAI 2004WO-US14002             20040505
CLASS
 PATENT NO.       CLASS  PATENT FAMILY CLASSIFICATION CODES
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 WO 2005112918    ICM    A61K-0031/40
                  ICS    A61K-0031/44
                  IPCI   A61K0031-40 [ICM,7]; A61K0031-44 [ICS,7]
OS   MARPAT 144:583
AB   Methods of treating, preventing and/or managing cancer as well as and
     diseases and disorders associated with, or characterized by, undesired
     angiogenesis are disclosed.  Specific methods encompass the administration
     of a selective cytokine inhibitory drug alone or in combination with a
     second active ingredient.  The invention further relates to methods of
     reducing or avoiding adverse side effects associated with chemotherapy,
     radiation therapy, hormonal therapy, biol. therapy or immunotherapy which
     comprise the administration of a selective cytokine inhibitory drug.
     Pharmaceutical compns., single unit dosage forms, and kits suitable for
     use in methods of the invention are also disclosed.
ST   antitumor cytokine inhibitor cancer therapy
IT   Lymphoma
       (B-cell diffuse, large cell; cytokine inhibitors for treatment and
       management of cancers and other diseases)
IT   Lymphoma
       (B-cell, cutaneous; cytokine inhibitors for treatment and management of
       cancers and other diseases)
IT   Inflammation
       (Crohn's disease; cytokine inhibitors for treatment and management of
       cancers and other diseases)
IT   Intestine, disease
       (Crohn's; cytokine inhibitors for treatment and management of cancers
       and other diseases)
IT   Heat-shock proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
```

(HSP 90, inhibitors; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Sarcoma
(Kaposi's; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Mammary gland, neoplasm
(Paget's disease; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Bone, disease
(Paget's; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Skin, neoplasm
(T-cell lymphoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(VEGFR, HER-2; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Lymphoproliferative disorders
(Waldenstrom's macroglobulinemia; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Sarcoidosis
(Wegener's sarcoidosis; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Neuroglia, neoplasm
(anaplastic astrocytoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT neu (receptor)
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Drug resistance
(antitumor; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Infection
(bacterial, bacterial ulcer; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Ulcer
(bacterial, fungal, Mooren; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Therapy
(biol. therapy; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Carcinoma
(bladder transitional cell, metastatic; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Transplant and Transplantation
(bone marrow; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Oviduct
(cancer; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Artery, disease
(carotid, occlusion; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Eye, disease
(chronic vitritis, choroiditis, optic pits; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Intestine, neoplasm
(colorectal carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Carcinoma
Intestine, neoplasm
(colorectal; cytokine inhibitors for treatment and management of

cancers and other diseases)
IT Eye
(cornea, transplant; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Transplant and Transplantation
(cornea; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Lymphoma
(cutaneous T-cell; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Acute myeloid leukemia
Amyloidosis
**Angiogenesis**
**Angiogenesis inhibitors**
Anti-inflammatory agents
Antiarthritics
Antibiotics
Antiglaucoma agents
Antirheumatic agents
Antitumor agents
Antiulcer agents
Behcet's syndrome
Bladder, neoplasm
Brain, neoplasm
Cardiovascular agents
Cord blood
Drug delivery systems
Endotoxemia
Fibrosis
Hematopoietic precursor cell
Hodgkin's disease
Human
Human herpesvirus
Human herpesvirus 3
Immunomodulators
Immunosuppressants
Immunotherapy
Lyme disease
Melanoma
Meningitis
Multiple myeloma
Neoplasm
Neuroglia, neoplasm
Osteoarthritis
Prophylaxis
Prostate gland, neoplasm
Radiotherapy
Retroviridae
Rheumatoid arthritis
Shock (circulatory collapse)
Sickle cell anemia
Sjogren syndrome
Surgery
Syphilis
Transplant and Transplantation
Transplant rejection
(cytokine inhibitors for treatment and management of cancers and other diseases)
IT Insulin-like growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cytokine inhibitors for treatment and management of cancers and other diseases)
IT Cytokines
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other

diseases)
IT Corticosteroids, biological studies
Hemopoietins
Interferons
Interleukin 2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other diseases)
IT Eye, disease
(diabetic retinopathy; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Reticuloendothelial system
(disease, histiocytosis, Langerhans cell; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Uterus, disease
(endometriosis; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Heart, disease
Kidney, disease
(failure; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Asbestos
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(fibrosis from; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Thyroid gland, neoplasm
(follicular cell carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Fungi
(fungal ulcer; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Gingiva, disease
Inflammation
(gingivitis; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Neuroglia, neoplasm
(glioblastoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Sarcoma
(gynecol.; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Blood vessel, neoplasm
(hemangiopericytoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Carcinoma
(hepatocellular; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Liver, neoplasm
(hepatoma, metastatic; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Liver, neoplasm
(hepatoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Infection
(herpes simplex; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Infection
(herpes zoster; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Disease, animal
(histiocytosis, Langerhans cell; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Hormones, animal, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hormonal therapy; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Neoplasm
(humoral hypercalcemia of malignancy; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Protozoa
(infection; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Epidermal growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Eye, disease
Inflammation
(keratitis; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Eye, disease
Inflammation
(keratoconjunctivitis, epidemic; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Myoma
(leiomyoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Myoma
Sarcoma
(leiomyosarcoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lipid degeneration; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Anemia (disease)
(macrocytic anemia; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Thyroid gland, neoplasm
(medullary carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Nervous system, neoplasm
(meningioma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Mesothelium, neoplasm
(mesothelioma, malignant pleural effusion mesothelioma syndrome; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Brain, neoplasm
(metastasis; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Mammary gland, neoplasm
Melanoma
(metastatic; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, inhibitors; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Erythema
(multiforme; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Vision disorders
(myopia; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Astrocyte
(neoplasm, anaplastic astrocytoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Meninges

(neoplasm, meningioma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Oligodendrocyte
(neoplasm, oligodendroglioma, anaplastic; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Glaucoma (disease)
(neovascular; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Nerve, neoplasm
(neuroblastoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Endocrine system, neoplasm
(neuroendocrine system; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Lymphoma
(nodular; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Lymphoma
(non-Hodgkin's; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Lung, neoplasm
(non-small-cell carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Artery, disease
Vein, disease
(occlusion; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Histoplasma capsulatum
(ocular histoplasmosis; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Neuroglia, neoplasm
(oligodendroglioma, anaplastic; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Thyroid gland, neoplasm
(papillary carcinoma, serous; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Skin, disease
(pemphigoid; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Inflammation
Periodontium, disease
(periodontitis; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Stem cell
(peripheral blood; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Eye, disease
(periretinal proliferation; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Peritoneum, neoplasm
(peritoneal carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Disease, animal
(phylectenulosis, fibrodysplasia ossificans, Terrien's marginal degeneration, Eale, best, stargart, pars planitis, hyperviscosity, rubeosis, 5q, mariginal keratolysis; cytokine inhibitors for treatment and management of cancers)
IT Placenta
(placental blood; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Artery, disease
(polyarteritis; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Infection
(protozoan; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Skin, neoplasm
(pseudoxanthoma elasticum; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Carcinoma
(pulmonary non-small-cell; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Eye
(radial keratotomy; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Carcinoma
(rectal adenocarcinoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Intestine, neoplasm
(rectum, adenocarcinoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Drug toxicity
(reduction of; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Anemia (disease)
(refractory; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Antitumor agents
(resistance to; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Eye, disease
(retina, detachment, chronic; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Eye, disease
Inflammation
(retinitis; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Eye, disease
(retrolental fibroplasia; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Skin, disease
(rosacea; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Eye, disease
Inflammation
(scleritis; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Connective tissue, disease
(scleroderma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Biliary tract, disease
Inflammation
(sclerosing cholangitis; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Animal tissue, disease
(soft, neoplasm, sarcoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Sarcoma
(soft-tissue; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Brain, disease
(stroke; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Lupus erythematosus
(systemic; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Carcinoma
(thyroid follicular cell; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Carcinoma
(thyroid medullary; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Carcinoma
(thyroid papillary, serous; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Shock (circulatory collapse)
(toxic shock syndrome; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Infection
(toxoplasmosis; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Eye, disease
(trachoma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Bladder, neoplasm
(transitional cell carcinoma, metastatic; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Bone marrow
(transplant; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Injury
(trauma; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Eye, disease
Inflammation
(uveitis, chronic; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Blood vessel, disease
Inflammation
(vasculitis, cutaneous; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Drugs
(veterinary; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Infection
(viral, HSV; cytokine inhibitors for treatment and management of cancers and other diseases)
IT Disease, animal
(wasting; cytokine inhibitors for treatment and management of cancers and other diseases)
IT 167886-76-2
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other diseases)
IT 50-02-2, Dexamethasone 57-22-7, Vincristine 147-94-4, Ara-C 148-82-3, Melphalan 362-07-2, 2-Methoxyestradiol 564-25-0, Doxycycline 4342-03-4, Dacarbazine 4759-48-2, Isotretinoin 6493-05-6, Pentoxifylline 11096-26-7, EPO 19545-26-7, Wortmannin 23214-92-8, Doxorubicin 71486-22-1, Vinorelbine 83869-56-1, Granulocyte-macrophage colony-stimulating factor 85721-33-1, Ciprofloxacin 97682-44-5, Irinotecan 114977-28-5, Taxotere 123948-87-8, Topotecan 143011-72-7, Granulocyte colony-stimulating factor 156586-89-9, Edrecolomab 174722-31-7, Rituximab 179324-69-7, Bortezomib 180288-69-1, Trastuzumab 183321-74-6, Erlotinib 184475-35-2, Gefitinib 185243-69-0, Etanercept 190977-41-4, Oblimersen 194413-58-6, Semaxanib 208921-02-2, Tositumomab 216974-75-3, Bevacizumab 265114-54-3, Telomestatin 340019-67-2 380610-27-5, Pertuzumab
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other diseases)
IT 9028-35-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, statins; cytokine inhibitors for treatment and management of cancers and other diseases)
IT 9067-71-4, Lysophosphatidic acid acyltransferase 9076-57-7, Histone deacetylase 103843-29-4, Insulin-like growth factor-I receptor kinase

115926-52-8, PI3 kinase 137632-03-2, c-Met Tyrosine kinase
159606-08-3, IκB Kinase 165245-96-5, p38 MAP kinase 329900-75-6,
Cox-2 386705-49-3, Vascular endothelial growth factor receptor kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; cytokine inhibitors for treatment and management of cancers and other diseases)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

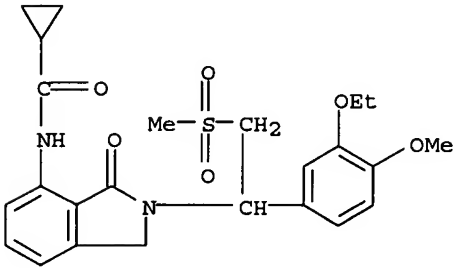
RE

(1) Duggan, M; US---6268378 B1 2001 HCAPLUS
(2) Zeldis; US2003438213 A1 2003
(3) Zeldis, J; WO2003097040 A1 2003 HCAPLUS

IT 340019-67-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other diseases)

RN 340019-67-2 HCAPLUS

CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)




L17 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:428800 HCAPLUS

DN 140:417925

ED Entered STN: 27 May 2004

TI Methods and compositions using selective cytokine inhibitory drugs for treatment and management of cancers and other diseases

IN **Zeldis, Jerome B.**

PA **Celgene** Corporation, USA

SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K

CC 1-6 (Pharmacology)
Section cross-reference(s): 63

FAN.CNT 5

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO2004043378 | A2 | 20040527 | WO 2003-US335545 | 20031106 |
| WO2004043378 | A3 | 20040902 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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| CA---2505131 | AA | 20040527 | 2003CA-2505131 | 20031106 <-- |
| AU2003290652 | A1 | 20040603 | 2003AU-0290652 | 20031106 <-- |
| EP---1567154 | A2 | 20050831 | 2003EP-0783234 | 20031106 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR2003016057 | A | 20050920 | 2003BR-0016057 | 20031106 <-- |
| CN---1735412 | A | 20060215 | CN 2003-80108390 | 20031106 |
| JP2006508131 | T2 | 20060309 | 2004JP-0551873 | 20031106 <-- |
| US2006035955 | A1 | 20060216 | 2005US-0534325 | 20050912 <-- |
| AU2006202316 | A1 | 20060622 | 2006AU-0202316 | 20060531 |
| PRAI 2002US-424601P | P | 20021106 | | |
| 2003AU-0234626 | A3 | 20030516 | | |
| 2003WO-US35545 | W | 20031106 <-- | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| WO 2004043378 | ICM | A61K |
| | IPCI | A61K [ICM,7] |
| | IPCR | A61K0031-00 [I,A]; A61K0031-00 [I,C*]; A61K0031-40 [I,A]; A61K0031-40 [I,C*]; A61K0031-425 [I,A]; A61K0031-425 [I,C*]; A61K0031-445 [I,A]; A61K0031-445 [I,C*]; A61K0031-513 [I,C*]; A61K0031-515 [I,A]; A61K0045-00 [I,C*]; A61K0045-06 [I,A] |
| | ECLA | A61K031/00; A61K031/40; A61K031/425; A61K031/445; A61K031/515; A61K045/06; A61K031/40+M; A61K031/4035; A61K031/4035+M; A61K031/415; A61K031/415+M; A61K031/425+M; A61K031/44; A61K031/44+M; A61K031/454; A61K031/454+M |
| CA---2505131 | IPCI | A61K0031-44 [ICM,7]; A61K0031-40 [ICS,7]; A61K0031-415 [ICS,7]; A61K0031-425 [ICS,7] |
| | IPCR | A61K0031-00 [I,A]; A61K0031-00 [I,C*]; A61K0031-40 [I,A]; A61K0031-40 [I,C*]; A61K0031-425 [I,A]; A61K0031-425 [I,C*]; A61K0031-445 [I,A]; A61K0031-445 [I,C*]; A61K0031-513 [I,C*]; A61K0031-515 [I,A]; A61K0045-00 [I,C*]; A61K0045-06 [I,A] |
| | ECLA | A61K031/40; A61K031/00; A61K031/40+M; A61K031/4035; A61K031/4035+M; A61K031/415; A61K031/415+M; A61K031/425; A61K031/425+M; A61K031/44; A61K031/44+M; A61K031/454; A61K031/454+M; A61K045/06 |
| AU2003290652 | IPCI | A61K0031-44 [ICM,7]; A61K0031-425 [ICS,7]; A61K0031-415 [ICS,7]; A61K0031-40 [ICS,7] |
| | IPCR | A61K0031-00 [I,A]; A61K0031-00 [I,C*]; A61K0031-40 [I,A]; A61K0031-40 [I,C*]; A61K0031-425 [I,A]; A61K0031-425 [I,C*]; A61K0031-445 [I,A]; A61K0031-445 [I,C*]; A61K0031-513 [I,C*]; A61K0031-515 [I,A]; A61K0045-00 [I,C*]; A61K0045-06 [I,A] |
| EP---1567154 | IPCI | A61K0031-44 [ICM,7]; A61K0031-425 [ICS,7]; A61K0031-415 [ICS,7]; A61K0031-40 [ICS,7] |
| | IPCR | A61K0031-00 [I,A]; A61K0031-00 [I,C*]; A61K0031-40 [I,A]; A61K0031-40 [I,C*]; A61K0031-425 [I,A]; A61K0031-425 [I,C*]; A61K0031-445 [I,A]; A61K0031-445 [I,C*]; A61K0031-513 [I,C*]; A61K0031-515 [I,A]; A61K0045-00 [I,C*]; A61K0045-06 [I,A] |
| | ECLA | A61K031/40; A61K031/00; A61K031/40+M; A61K031/4035; A61K031/4035+M; A61K031/415; A61K031/415+M; A61K031/425; A61K031/425+M; A61K031/44; A61K031/44+M; A61K031/454; A61K031/454+M; A61K045/06 |
| BR2003016057 | IPCI | A61K0031-44 [ICM,7]; A61K0031-425 [ICS,7]; A61K0031-415 [ICS,7]; A61K0031-40 [ICS,7] |
| | IPCR | A61K0031-00 [I,A]; A61K0031-00 [I,C*]; A61K0031-40 [I,A]; A61K0031-40 [I,C*]; A61K0031-425 [I,A]; A61K0031-425 [I,C*]; A61K0031-445 [I,A]; A61K0031-445 [I,C*]; A61K0031-513 [I,C*]; A61K0031-515 [I,A]; A61K0045-00 [I,C*]; A61K0045-06 [I,A] |
| | ECLA | A61K031/40; A61K031/00; A61K031/40+M; A61K031/4035; A61K031/4035+M; A61K031/415; A61K031/415+M; |

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|---|---|---|
| | | A61K031/425; A61K031/425+M; A61K031/44; A61K031/44+M; A61K031/454; A61K031/454+M; A61K045/06 |
| CN---1735412 | IPCI | A61K0031-44 [I,A]; A61K0031-425 [I,A]; A61K0031-415 [I,A]; A61K0031-40 [I,A] |
| | ECLA | A61K031/40; A61K031/00; A61K031/40+M; A61K031/4035; A61K031/4035+M; A61K031/415; A61K031/415+M; A61K031/425; A61K031/425+M; A61K031/44; A61K031/44+M; A61K031/454; A61K031/454+M; A61K045/06 |
| JP2006508131 | IPCI | A61K0045-00 [I,A]; A61K0031-4035 [I,A]; A61K0031-403 [I,C*]; A61P0035-00 [I,A]; A61P0043-00 [I,A] |
| | FTERM | 4C084/AA17; 4C084/MA01; 4C084/NA14; 4C084/ZB052; 4C084/ZB212; 4C084/ZB262; 4C086/AA01; 4C086/AA02; 4C086/BC10; 4C086/MA01; 4C086/MA04; 4C086/NA14; 4C086/ZB05; 4C086/ZB21; 4C086/ZB26 |
| US2006035955 | IPCI | A61K0031-4035 [I,A]; A61K0031-403 [I,C*]; A61K0038-19 [I,A]; A61K0031-522 [I,A]; A61K0031-519 [I,C*] |
| | NCL | 514/416.000 |
| AU2006202316 | IPCI | A61K0031-00 [I,C*]; A61K0031-40 [I,C*]; A61K0031-425 [I,C*]; A61K0031-445 [I,C*]; A61K0031-4523 [I,C*]; A61K0031-513 [I,C*]; A61K0045-00 [I,C*]; A61K0031-445 [I,A]; A61K0031-00 [I,A]; A61K0031-40 [I,A]; A61K0031-425 [I,A]; A61K0031-454 [I,A]; A61K0031-515 [I,A]; A61K0045-06 [I,A] |

OS MARPAT 140:417925

AB Methods for treating, preventing and/or managing cancer as well as and diseases and disorders associated with, or characterized by, undesired angiogenesis are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug alone or in combination with a second active ingredient. The invention further discloses methods for reducing or avoiding adverse side effects associated with chemotherapy, radiation therapy, hormonal therapy, biol. therapy or immunotherapy which comprise the administration of a selective cytokine inhibitory drug. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

ST antitumor drug therapeutic cytokine inhibitor angiogenesis inhibition; adverse effect redn therapeutic cytokine inhibitor

IT Disease, animal
(5q- syndrome; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Lymphoma
(B-cell diffuse, large cell; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Lymphoma
(B-cell, cutaneous; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Disease, animal
(Best; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Disease, animal
(Eale; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Sarcoma
(Kaposi's; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Ulcer
(Mooren; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Mammary gland, neoplasm
(Paget's disease; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Bone, disease
(Paget's; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Disease, animal
(Scleritis; cytokine inhibitors for treatment and management of cancers

and other diseases, and use with other thrapeutic means)
IT Disease, animal
(Stargart; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Skin, neoplasm
(T-cell lymphoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Disease, animal
(Terrien's marginal degeneration; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Lymphoproliferative disorders
(Waldenstrom's macroglobulinemia; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Disease, animal
(Wegener's sarcoidosis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Neuroglia, neoplasm
(anaplastic astrocytoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Drug resistance
(antitumor; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Infection
(bacterial, bacterial ulcer; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Therapy
(biol. therapy; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Carcinoma
(bladder transitional cell, metastatic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Transplant and Transplantation
(bone marrow; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Oviduct
(cancer; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Artery, disease
(carotid, occlusion; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Eye, disease
(choroiditis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Eye, disease
(chronic vitritis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Intestine, neoplasm
(colorectal carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Carcinoma
Intestine, neoplasm
(colorectal; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Eye
(cornea, transplant; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Transplant and Transplantation
(cornea; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Lymphoma

(cutaneous T-cell; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Acute myeloid leukemia
Amyloidosis
**Angiogenesis**
**Angiogenesis inhibitors**
Anti-inflammatory agents
Antiarthritics
Antibiotics
Antiglaucoma agents
Antirheumatic agents
Antitumor agents
Antiulcer agents
Behcet's syndrome
Bladder, neoplasm
Brain, neoplasm
Cardiovascular agents
Cord blood
Drug delivery systems
Endotoxemia
Fibrosis
Hematopoietic precursor cell
Hodgkin's disease
Human
Human herpesvirus
Human herpesvirus 3
Immunomodulators
Immunosuppressants
Immunotherapy
Lyme disease
Melanoma
Meningitis
Multiple myeloma
Neoplasm
Neuroglia, neoplasm
Osteoarthritis
Prostate gland, neoplasm
Radiotherapy
Rheumatoid arthritis
Shock (circulatory collapse)
Sickle cell anemia
Sjogren syndrome
Surgery
Syphilis
Transplant and Transplantation
Transplant rejection
Ulcer
(cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Cytokines
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Corticosteroids, biological studies
Hemopoietins
Interferons
Interleukin 2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Eye, disease
(diabetic retinopathy; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Reticuloendothelial system

(disease, histiocytosis, Langerhans cell; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Disease, animal
(fibrodysplasia ossificans; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Asbestos
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(fibrosis from; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Thyroid gland, neoplasm
(follicular cell carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Fungi
(fungal ulcer; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Gingiva, disease
Inflammation
(gingivitis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Neuroglia, neoplasm
Neuroglia, neoplasm
(glioblastoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Sarcoma
(gynecol.; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Blood vessel, neoplasm
(hemangiopericytoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Carcinoma
(hepatocellular; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Liver, neoplasm
(hepatoma, metastatic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Liver, neoplasm
(hepatoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Disease, animal
(histiocytosis, Langerhans cell; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Hormones, animal, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hormonal therapy; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Neoplasm
(humoral hypercalcemia of malignancy; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Disease, animal
(hyperviscosity syndromes; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Protozoa
(infection; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Eye, disease
Inflammation
(keratitis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Eye, disease

Inflammation
(keratoconjunctivitis, epidemic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Myoma
(leiomyoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Myoma
Sarcoma
(leiomyosarcoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lipid degeneration; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Anemia (disease)
(macrocytic anemia; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Disease, animal
(mariginal keratolysis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Thyroid gland, neoplasm
(medullary carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Nervous system, neoplasm
(meningioma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Mesothelium, neoplasm
(mesothelioma, malignant pleural effusion mesothelioma syndrome; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Brain, neoplasm
(metastasis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Mammary gland, neoplasm
Melanoma
(metastatic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Erythema
(multiforme; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Vision disorders
(myopia; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Astrocyte
(neoplasm, anaplastic astrocytoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Meninges
(neoplasm, meningioma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Oligodendrocyte
(neoplasm, oligodendroglioma, anaplastic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Glaucoma (disease)
(neovascular; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Nerve, neoplasm
(neuroblastoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Endocrine system, neoplasm
(neuroendocrine system; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Lymphoma
(nodular; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Lymphoma
(non-Hodgkin's; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Lung, neoplasm
(non-small-cell carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Artery, disease
Vein, disease
(occlusion; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Histoplasma capsulatum
(ocular histoplasmosis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Neuroglia, neoplasm
(oligodendroglioma, anaplastic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Eye, disease
(optic pits; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Thyroid gland, neoplasm
(papillary carcinoma, serous; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Disease, animal
(pars planitis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Skin, disease
(pemphigoid; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Inflammation
Periodontium, disease
(periodontitis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Stem cell
(peripheral blood; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Eye, disease
(periretinal proliferation; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Peritoneum, neoplasm
(peritoneal carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Disease, animal
(phylectenulosis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Placenta
(placental blood; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Artery, disease
(polyarteritis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Skin, neoplasm
(pseudoxanthoma elasticum; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Carcinoma
(pulmonary non-small-cell; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

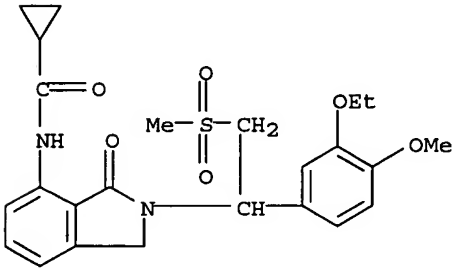
IT Eye
(radial keratotomy; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Carcinoma
(rectal adenocarcinoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Intestine, neoplasm
(rectum, adenocarcinoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Drug toxicity
(reduction of; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Anemia (disease)
(refractory; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Antitumor agents
(resistance to; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Eye, disease
(retina, detachment, chronic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Eye, disease
Inflammation
(retinitis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Eye, disease
(retrolental fibroplasia; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Retroviridae
(retrovirus replication; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Skin, disease
(rosacea; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Disease, animal
(rubeosis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Disease, animal
(sarcoid; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Connective tissue, disease
(scleroderma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Biliary tract, disease
Inflammation
(sclerosing cholangitis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Animal tissue, disease
(soft, neoplasm, sarcoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Sarcoma
(soft-tissue; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Brain, disease
(stroke; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Lupus erythematosus
(systemic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

IT Carcinoma
(thyroid follicular cell; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Carcinoma
(thyroid medullary; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Carcinoma
(thyroid papillary, serous; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Shock (circulatory collapse)
(toxic shock syndrome; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Infection
(toxoplasmosis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Eye, disease
(trachoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Bladder, neoplasm
(transitional cell carcinoma, metastatic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Bone marrow
(transplant; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Injury
(trauma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Eye, disease
Inflammation
(uveitis, chronic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Blood vessel, disease
Inflammation
(vasculitis, cutaneous; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Drugs
(veterinary; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT Disease, animal
(wasting; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT 50-02-2, Dexamethasone 57-22-7, Vincristine 147-94-4, Ara-C 148-82-3, Melphalan 4342-03-4, Dacarbazine 4759-48-2, Isotretinoin 6493-05-6, Pentoxifylline 11096-26-7, Erythropoietin 23214-92-8, Doxorubicin 71486-22-1, Vinorelbine 83869-56-1, GM-CSF 85721-33-1, Ciprofloxacin 97682-44-5, Irinotecan 114977-28-5, Taxotere 123948-87-8, Topotecan 143011-72-7, G-CSF 167886-76-2 190977-41-4, Oblimersen **340019-67-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT 7631-86-9, Silica, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(fibrosis from; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT 329900-75-6, Cyclooxygenase 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)
IT **340019-67-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

RN 340019-67-2 HCAPLUS

CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



L17 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:392056 HCAPLUS

DN 140:386062

ED Entered STN: 14 May 2004

TI Methods of using and compositions comprising selective cytokine inhibitory drugs for treatment and management of macular degeneration

IN **Zeldis, Jerome B.**

PA USA

SO U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO

DT Patent

LA English

IC ICM A61K-0038/21
ICS A61K-0039/395; A61K-0031/56; A61K-0031/545; A61K-0031/522; A61K-0031/454; A61K-0031/557

INCL 424085700; 424145100; 514171000; 514200000; 514012000; 514192000; 514263310; 514323000; 514573000

CC 1-12 (Pharmacology)
Section cross-reference(s): 63

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US2004091454 | A1 | 20040513 | 2003US-0699110 | 20031030 |
| CA---2504263 | AA | 20040521 | 2003CA-2504263 | 20031031 |
| WO2004041181 | A2 | 20040521 | 2003WO-US34535 | 20031031 |
| WO2004041181 | A3 | 20050217 | | |
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| JP2006509743 | T2 | 20060323 | 2004JP-0550274 | 20031031 |

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    WO2005044269          A1    20050519    2004WO-US13253          20040428
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            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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            SN, TD, TG
PRAI 2002US-422900P        P     20021031
    2003US-0699110         A     20031030
    2003WO-US34535         W     20031031
    2004WO-US13253         W     20040428
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                  ICS    A61K-0039/395; A61K-0031/56; A61K-0031/545;
                         A61K-0031/522; A61K-0031/454; A61K-0031/557
                  INCL   424085700; 424145100; 514171000; 514200000; 514012000;
                         514192000; 514263310; 514323000; 514573000
                  IPCI   A61K0038-21 [ICM,7]; A61K0039-395 [ICS,7]; A61K0031-56
                         [ICS,7]; A61K0031-545 [ICS,7]; A61K0031-522 [ICS,7];
                         A61K0031-519 [ICS,7,C*]; A61K0031-454 [ICS,7];
                         A61K0031-4523 [ICS,7,C*]; A61K0031-557 [ICS,7]
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                         A61K0031-545 [I,C*]; A61K0031-557 [I,A]; A61K0031-557
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                  NCL    424/085.700
                  ECLA   A61K031/454; A61K031/522; A61K031/545; A61K031/557;
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| | IPCR | A61K0031-4523 [I,C*]; A61K0031-454 [I,A]; A61K0031-519 [I,C*]; A61K0031-522 [I,A]; A61K0031-545 [I,A]; A61K0031-545 [I,C*]; A61K0031-557 [I,A]; A61K0031-557 [I,C*]; A61K0031-56 [I,A]; A61K0031-56 [I,C*]; A61K0038-18 [I,A]; A61K0038-18 [I,C*]; A61K0038-21 [I,A]; A61K0038-21 [I,C*]; A61K0038-27 [I,A]; A61K0038-27 [I,C*] |
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| JP2006509743 | IPCI | A61K0045-00 [I,A]; A61K0031-4035 [I,A]; A61K0031-403 [I,C*]; A61K0031-409 [I,A]; A61K0031-454 [I,A]; A61K0031-4523 [I,C*]; A61K0045-06 [I,A]; A61P0009-00 [I,A]; A61P0009-10 [I,A]; A61P0027-02 [I,A]; A61P0027-00 [I,C*] |
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| WO2005044269 | IPCI | A61K0031-445 [ICM,7] |
| | IPCR | A61K0031-4523 [I,C*]; A61K0031-454 [I,A]; A61K0031-519 [I,C*]; A61K0031-522 [I,A]; A61K0031-545 [I,A]; A61K0031-545 [I,C*]; A61K0031-557 [I,A]; A61K0031-557 [I,C*]; A61K0031-56 [I,A]; A61K0031-56 [I,C*]; A61K0038-18 [I,A]; A61K0038-18 [I,C*]; A61K0038-21 [I,A]; A61K0038-21 [I,C*]; A61K0038-27 [I,A]; A61K0038-27 [I,C*] |
| | ECLA | A61K031/454; A61K031/522; A61K031/545; A61K031/557; A61K031/56; A61K038/18F+M; A61K038/21+M; A61K038/27+M |

OS MARPAT 140:386062

AB Methods of treating, preventing and/or managing macular degeneration are disclosed. Specific embodiments encompass the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or surgery. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed. Patients with macular degeneration were treated by photodynamic therapy with verteporfin alone, or with the addition of 20 mg/day of selective cytokine inhibitory drug (+)-2-[1-(3-ethoxy-4 methoxyphenyl)-2-methylsulfonylethyl]-4 acetylaminoisoindoline 1,3-dione. The neovascular cascade is sufficiently hindered in the group receiving (+)-2-[1-(3-ethoxy-4 methoxyphenyl)-2-methylsulfonylethyl]-4 acetylaminoisoindoline 1,3-dione to indefinitely prolong the effects of the photodynamic therapy.

ST selective cytokine inhibitory drug management macular degeneration

IT Eye, disease
(Behr's disease, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(Doyne's disease, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(Sorsby's disease, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Steroids, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiostatic, as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT **Angiogenesis inhibitors**
Anti-inflammatory agents
Antibiotics
Antioxidants
Photosensitizers, pharmaceutical
(as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Integrins
Interferons
Neurotrophic factors
Phytoestrogens
Prostaglandins
Steroids, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(atrophy of retinal pigment epithelium, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye
(foveal translocation; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(fundus flavimaculatus, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(honeycomb dystrophy, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Drugs
Surgery
(in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Tumor necrosis factors

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(macula, degeneration, Stargardt's disease, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(macula, degeneration, congenital, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(macula, degeneration; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(macula, senile degeneration, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(macular damage, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(macular dystrophy, juvenile, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(maculopathy, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT **Angiogenesis**
(**neovascularization, eye**, regulator of, as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(neovascularization, regulator of, as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT **Angiogenesis**
(**neovascularization, retinal**, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Solvates
Stereoisomers
(of selective cytokine inhibitory drugs; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Clathrates
Hydrates
Salts, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of selective cytokine inhibitory drugs; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye
(pigment epithelium, detachment or atrophy of, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

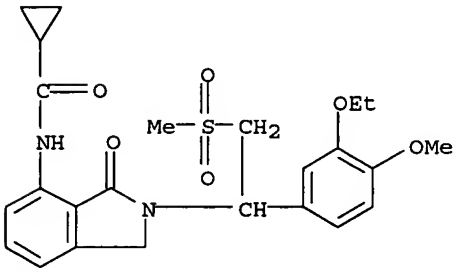
IT Drug delivery systems
(prodrugs, of selective cytokine inhibitory drugs; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(retina, detachment, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

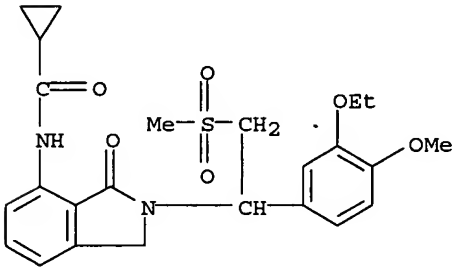
IT Eye, disease
(retina, neovascularization, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular

degeneration)
IT Eye
(retinal pigment epithelium transplant; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
IT Transplant and Transplantation
(retinal pigment epithelium; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
IT Epithelium
(retinal pigment, detachment or atrophy of, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
IT Drug delivery systems
Human
Phototherapy
Radiotherapy
(selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
IT Cytokines
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(selective inhibitors; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
IT Lasers
(therapy; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to VEGF, as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
IT Eye, disease
(vitelliform, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
IT Interferons
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α2, as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
IT **127464-60-2**, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibody to, as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
IT 50-35-1, Thalidomide 69-89-6D, Xanthine, derivs. 6493-05-6, Pentoxifylline 9002-72-6, Growth hormone 129497-78-5, Verteporfin 284041-10-7, Purlytin 688035-40-7, RhuFab
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
IT 167886-76-2 167886-76-2D, salts, solvates, stereoisomers
**340019-67-2** **340019-67-2D**, salts, solvates, stereoisomers
608141-41-9
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
IT **127464-60-2**, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibody to, as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
RN 127464-60-2 HCAPLUS
CN Vascular endothelial growth factor (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT 340019-67-2 340019-67-2D, salts, solvates, stereoisomers
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
RN 340019-67-2 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)




RN 340019-67-2 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)




L17 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:1001604 HCAPLUS
DN 140:42030
ED Entered STN: 24 Dec 2003
TI Preparation of isoindolinediones as angiogenesis inhibitors.
IN Man, Hon-wah; Muller, George W.
PA Celgene Corporation, USA
SO U.S., 28 pp., Cont.-in-part of U.S. Ser. No. 590,344.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07D-0413/04
ICS C07D-0403/04; C07D-0235/16; A61K-0031/4184; A61P-0035/00
INCL 514323000; 514383000; 514385000; 514412000; 514416000; 514417000; 546143000; 546266400; 546312100; 546466000
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 4

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     JP2004500346          T2    20040108    2001JP-0536553          20001109
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     NO2002002223          A     20020708    2002NO-0002223          20020508
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PRAI 1999US-165168P        P     19991112
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     2000WO-US30770        W     20001109
CLASS
 PATENT NO.       CLASS  PATENT FAMILY CLASSIFICATION CODES
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 US 6667316       ICM    C07D-0413/04
                  ICS    C07D-0403/04; C07D-0235/16; A61K-0031/4184;
                         A61P-0035/00
                  INCL   514323000; 514383000; 514385000; 514412000; 514416000;
                         514417000; 546143000; 546266400; 546312100; 546466000
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                         C07D0235-16 [ICS,7]; C07D0235-00 [ICS,7,C*];
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                         514/416.000; 514/417.000; 546/143.000
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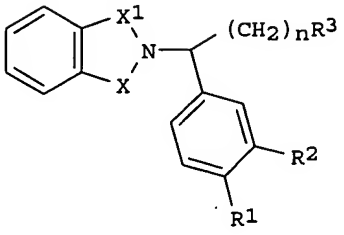
GI




I

AB Title compds. [I; R1, R2 = alkyl, alkoxy, cyano, cycloalkoxy, cycloalkyl, cycloalkylmethoxy; 1 of X and X1 = CO, SO2 and the other of X and X1 = CO, CH2, SO2, CH2CO; R3 = SO2Y, COZ, CN, hydroxyalkyl; Y = alkyl, Ph, PhCH2; Z = NR61R71, alkyl, Ph, PhCH2; R61 = H, alkyl, cycloalkyl, Ph, PhCH2, etc.; R71 = alkyl; 1 of R4, R5 = H and the other = imidazolyl, pyrrolyl, oxadiazolyl, triazolyl, R6R7N(CzH2z); z = 0, 1; n = 1-3; R6 = cycloalkanoyl which is unsubstituted or substituted with halo, amino, monoalkylamino, dialkylamino; R4R5 = NHCH2R8, NHCOR8, N:CHR8; R7 = H, alkyl, methylsulfonyl, alkoxyalkylcarbonyl; R8 = CH2, O, NH, CH:CH, CH:N], were prepared for treatment of undesirable angiogenesis (no data). Thus, 3,4-dinitrophthalic acid and 2-(3-ethoxy-4-methoxyphenyl)-1-(methylsulfonyl)eth-2-ylamine in PhMe were refluxed for 15 h through a Dean-Stark trap to give 49% 2-[1-(3-Ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4,5-dinitroisoindoline-1,3-dione. This was hydrogenated in EtOAc over Pd/C to give 73% 2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4,5-diaminoisoindoline-1,3-dione. The latter was refluxed 17 h with DMF di-Me acetal in HOAc to give 68% 7-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-3-pyrrolino[3,4-e]benzimidazole-6,8-dione.

ST isoindolinedione prepn angiogenesis inhibitor

IT **Angiogenesis**
**Angiogenesis inhibitors**
Human
(preparation of isoindolinediones as angiogenesis inhibitors)

IT 340019-32-1P 340019-79-6P 340019-81-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of isoindolinediones as angiogenesis inhibitors)

IT 340019-18-3P 340019-19-4P 340019-20-7P 340019-21-8P 340019-22-9P
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340019-83-2P 340019-84-3P 340019-85-4P 340019-86-5P 340019-87-6P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoindolinediones as angiogenesis inhibitors)

IT 75-16-1, Methylmagnesium bromide 75-36-5, Acetyl chloride 79-04-9 79-22-1, Methyl chloroformate 107-22-2, Glyoxal 108-24-7, Acetic anhydride 124-40-3, Dimethylamine, reactions 124-63-0, Methanesulfonyl chloride 407-25-0 530-62-1 563-76-8 696-59-3 4023-34-1, Cyclopropanecarbonyl chloride 4524-93-0, Cyclopentanecarbonyl chloride 4637-24-5, Dmf dimethyl acetal 6296-53-3, 3-Acetamidophthalic anhydride 15486-96-1 18871-66-4, Dimethylacetamide dimethyl acetal 32315-10-9, Triphosgene 92971-15-8, 3,4-Dinitrophthalic acid 143092-07-3, Furo[3,4-h]quinoline-7,9-dione 201408-36-8 253168-83-1 253168-94-4 340019-74-1 340019-97-8 340019-98-9 340019-99-0 340020-00-0 340020-01-1 340020-02-2 340020-03-3 340020-04-4 340020-05-5 340020-06-6 340020-07-7 635705-69-0 635705-70-3 635705-71-4 635705-72-5 635705-73-6 635705-74-7 635705-75-8 635705-76-9 635705-77-0 635705-78-1 635705-79-2 635705-80-5 635705-81-6 635705-82-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of isoindolinediones as angiogenesis inhibitors)

IT 340019-16-1P 340019-17-2P 340019-34-3P 340019-35-4P 340019-36-5P 340019-37-6P 340019-38-7P 340019-77-4P 340019-91-2P 340019-92-3P 340019-93-4P 340019-94-5P 340019-95-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of isoindolinediones as angiogenesis inhibitors)

RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD

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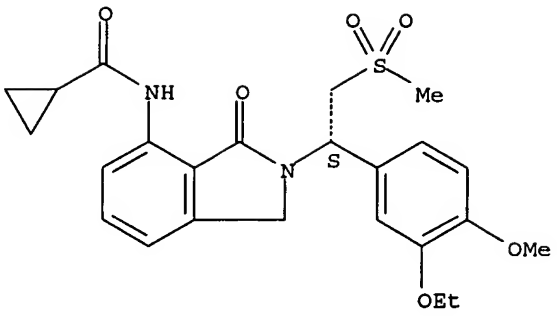

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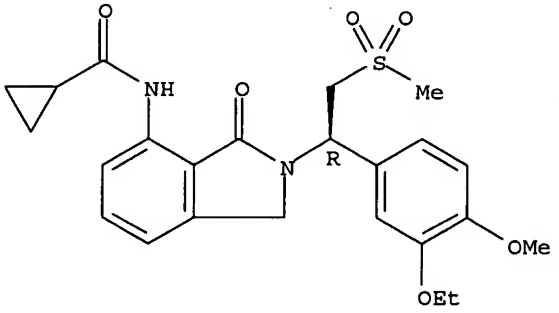
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

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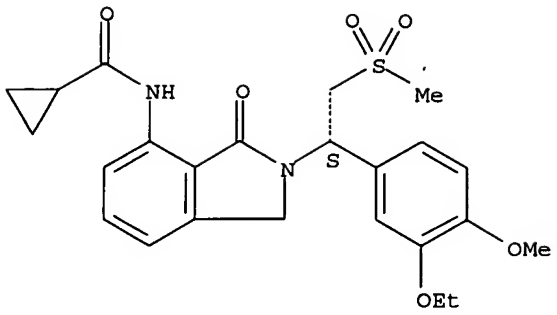
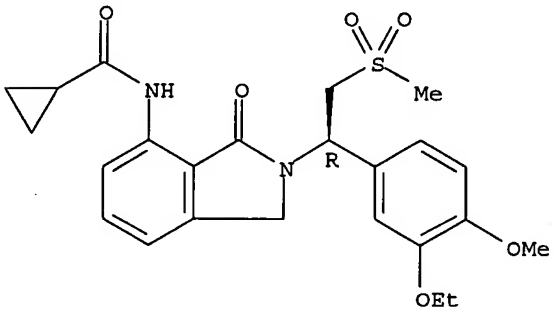
L22 ANSWER 1 OF 2 USPATFULL on STN
AN 2004:120049 USPATFULL
TI Methods of using and compositions comprising selective cytokine inhibitory drugs for treatment and management of macular degeneration
IN Zeldis, Jerome B., Princeton, NJ, UNITED STATES
PI US2004091454 A1 20040513
AI 2003US-0699110 A1 20031030 (10)
PRAI 2002US-422900P 20021031 (60)
DT Utility
FS APPLICATION
LREP JONES DAY, 222 EAST 41ST STREET, NEW YORK, NY, 10017
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1771
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of treating, preventing and/or managing macular degeneration are disclosed. Specific embodiments encompass the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable



RN 340019-70-7 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:359998 HCAPLUS
DN 134:366799
ED Entered STN: 18 May 2001
TI Preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases
IN Man, Hon-Wah; Muller, George
PA **Celgene** Corporation, USA
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D-0487/04
ICS C07D-0471/04; C07D-0413/04; C07D-0403/04; C07D-0209/46; C07D-0209/48; C07D-0209/49; A61K-0031/4188; A61K-0031/437; A61K-0031/4985; A61K-0031/4245; A61K-0031/4196; A61K-0031/4178; A61K-0031/4035; A61P-0011/06
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 4

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| PI WO2001034606 | A1 | 20010517 | 2000WO-US30770 | 20001109 |

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OS MARPAT 134:366799

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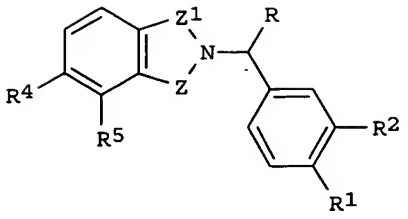

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AB Title compds. [I; R = (CnH2n)R3; R1,R2 = (cyclo)alkyl(oxy), cyano, cycloalkylmethoxy; R3 = hydroxyalkyl, cyano, SO2R6, COR7; 1 of R4,R5 = H and the other = pyrrolyl, imidazolyl, (un)substituted amino(alkyl), etc.; R4,R5 = (un)substituted amino(alkyl); R4R5 = atoms to complete a ring; R6 = alkyl, Ph, CH2Ph; R7 = groups cited for R6, (un)substituted amino; 1 of Z,Z1 = CO or SO2 and the other = CH2, CO, SO2, CH2CO; n = 1-3] were prepared for treatment of phosphodiesterase- and TNFα-mediated diseases (no data). Thus, 3,4-dinitrophthalic acid was cyclocondensed with H2NCH(CH2SO2Me)C6H3(OEt)(OMe)-3,4 and the product reduced to give I (R = CH2SO2Me, R1 = OMe, R2 = OEt, R4 = R5 = NH2, Z = Z1 = CO).

ST isoindolinones prepn treatment phosphodiesterase TNFalpha mediated disease

IT **Angiogenesis inhibitors**
Antitumor agents
(preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases)

IT Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases)

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340019-46-7P 340019-48-9P 340019-51-4P 340019-53-6P 340019-81-0P
340019-83-2P 340019-87-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases)

IT 340019-18-3P 340019-19-4P 340019-20-7P 340019-21-8P 340019-22-9P
340019-24-1P 340019-25-2P 340019-26-3P 340019-27-4P 340019-28-5P
340019-29-6P 340019-30-9P 340019-31-0P 340019-33-2P 340019-41-2P
340019-45-6P 340019-47-8P 340019-49-0P 340019-50-3P 340019-52-5P
340019-54-7P 340019-55-8P 340019-56-9P 340019-57-0P 340019-58-1P
340019-59-2P 340019-60-5P 340019-61-6P 340019-62-7P 340019-63-8P
340019-64-9P 340019-65-0P 340019-66-1P **340019-67-2P**
340019-68-3P **340019-69-4P** **340019-70-7P** 340019-71-8P
340019-72-9P 340019-73-0P 340019-74-1P 340019-75-2P 340019-76-3P
340019-77-4P 340019-78-5P 340019-79-6P 340019-80-9P 340019-82-1P
340019-84-3P 340019-85-4P 340019-86-5P 340019-88-7P 340019-89-8P
340019-90-1P 340019-95-6P 340019-96-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases)

IT 9036-21-9, Phosphodiesterase-IV 141907-41-7, Matrix Metalloproteinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases)

IT 696-59-3, 2,5-Dimethoxytetrahydrofuran 4023-34-1, Cyclopropanecarbonyl chloride 4524-93-0, Cyclopentanecarbonyl chloride 6296-53-3, 3-Acetamidophthalic anhydride 7148-74-5, 2-Bromopropionyl chloride

15486-96-1, 3-Bromopropionyl chloride 92971-15-8, 3,4-Dinitrophthalic acid 143092-07-3, Furo[3,4-h]quinoline-7,9-dione 201408-36-8 253168-83-1 253168-94-4 340019-97-8 340019-98-9 340019-99-0 340020-00-0 340020-01-1 340020-02-2, 3-Amino-N-ethoxycarbonylphthalimide 340020-03-3 340020-04-4 340020-05-5 340020-06-6 340020-07-7 340020-08-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases)

IT 340019-16-1P 340019-34-3P 340019-35-4P 340019-36-5P 340019-37-6P 340019-38-7P 340019-91-2P 340019-92-3P 340019-93-4P 340019-94-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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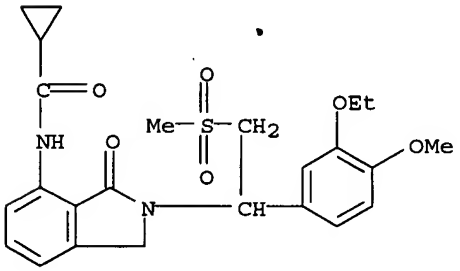
(2) Giembycz, M; Drugs 2000, V59(2), P193 HCAPLUS
(3) He, W; Novel Cyclic Compounds as potent Phosphodiesterase 4 Inhibitors 1998, V41(22), P4216 HCAPLUS
(4) Muller, G; Bioorg Med Chem Let 1998, V8, P2669 HCAPLUS
(5) Muller, G; J Med Chem 1996, V39, P3238 HCAPLUS

IT **340019-67-2P 340019-69-4P 340019-70-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases)

RN 340019-67-2 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)




RN 340019-69-4 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

(33) Muller; US---5703098 A 1997 HCAPLUS
(34) Muller; US---5728844 A 1998 HCAPLUS
(35) Muller; US---5728845 A 1998 HCAPLUS
(36) Muller; US---5736570 A 1998 HCAPLUS
(37) Muller; US---5801195 A 1998 HCAPLUS
(38) Muller; US---5877200 A 1999 HCAPLUS
(39) Muller; US---5929117 A 1999 HCAPLUS
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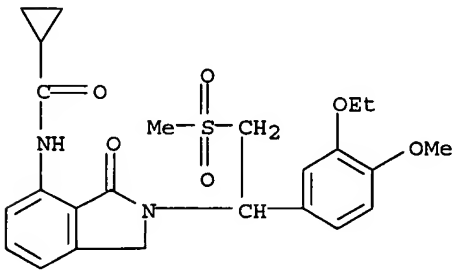
IT **340019-67-2P 340019-69-4P 340019-70-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoindolinediones as angiogenesis inhibitors)

RN 340019-67-2 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

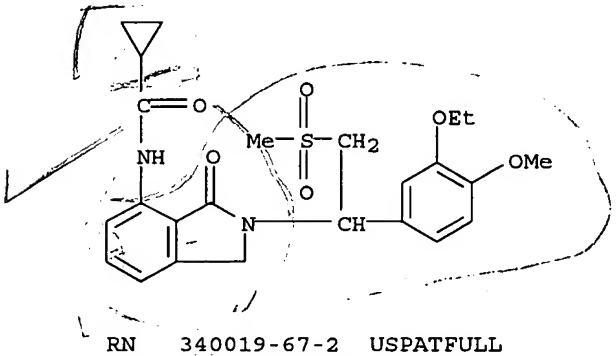



RN 340019-69-4 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

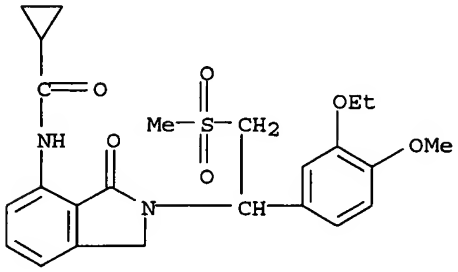
Absolute stereochemistry.

salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or surgery. Pharmaceutical compositions, single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **340019-67-2 340019-67-2D**, salts, solvates, stereoisomers
(selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
RN 340019-67-2 USPATFULL
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



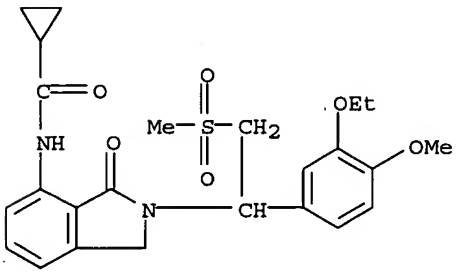

RN 340019-67-2 USPATFULL
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)




L22 ANSWER 2 OF 2 USPATFULL on STN
AN 2003:332383 USPATFULL
TI Pharmaceutically active isoindoline derivatives
IN Man, Hon-Wah, Princeton, NJ, United States
Muller, George W, Bridgewater, NJ, United States
PA Celgene Corporation, Warren, NJ, United States (U.S. corporation)
PI US---6667316 B1 20031223
AI 2000US-0708199 20001108 (9)
RLI Continuation-in-part of Ser. No. 2000US-0590344, filed on 8 Jun 2000
PRAI 1999US-165168P 19991112 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: McKenzie, Thomas
LREP Mathews, Collins, Shepherd & McKay, P.A.
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)

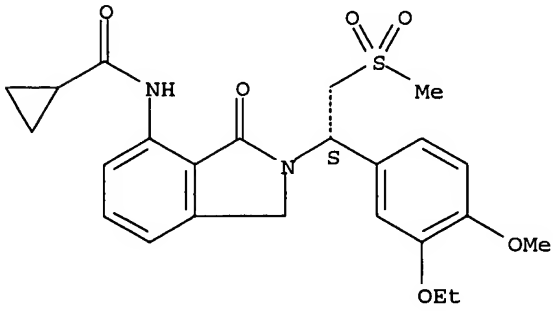
LN.CNT 2999
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound of formula I wherein each of R.sup.1 and R.sup.2, independently of the other, is alkyl, alkoxy, cyano, cycloalkoxy, cycloalkyl or cycloalkylmethoxy; one of X and X' is .dbd.C.dbd.O or .dbd.SO.sub.2 and the other of X and X' is a divalent group selected from .dbd.C.dbd.O, .dbd.CH.sub.2, .dbd.SO.sub.2 or .dbd.CH.sub.2C.dbd.O; R.sup.3 is --SO.sub.2--Y, --COZ, --CN, or hydroxyalkyl in which Y is alkyl, phenyl, or benzyl and Z is --NR.sup.6"R.sup.7", alkyl, phenyl, or benzyl; one of R.sup.4 and R.sup.5 is hydrogen and the other of R.sup.4 and R.sup.5 is imidazolyl, pyrrolyl; oxadiazolyl, triazolyl, or R.sup.6R.sup.7N(C.sub.zH.sub.2z)-- wherein R.sup.6, when taken independently of R.sup.7, is cycloalkanoyl which is unsubstituted or substituted with halo, amino, monoalkylamino or dialkylamino; and R.sup.7 is hydrogen, alkyl of 1 to 4 carbon atoms, methylsufonyl; or alkoxyalkylcarbonyl. Compounds of the present invention are useful as inhibitors of TNFα, PDE 4, matrix metalloproteases, and angiogenesis, and for treating cancer, autoimmune disease, and inflammatory disease. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **340019-67-2P 340019-69-4P 340019-70-7P**
(preparation of isoindolinediones as angiogenesis inhibitors)
RN 340019-67-2 USPATFULL
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)




RN 340019-69-4 USPATFULL
CN Cyclopropanecarboxamide, N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

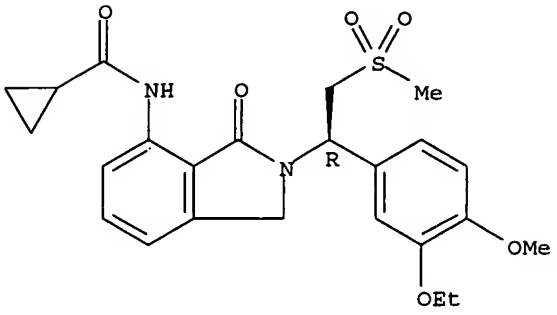
Absolute stereochemistry.




RN 340019-70-7 USPATFULL
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA

INDEX NAME)

Absolute stereochemistry.

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=> d all dcn dcre abex tech l42 tot

L42  ANSWER 1 OF 5  WPIX  COPYRIGHT 2006 THE THOMSON CORP on STN
AN   2005-746262 [76]   WPIX
DNC  C2005-227366
TI   Use of phosphodiesterase-4 modulators for treatment, prevention, or
     managing pulmonary hypertension and associated symptoms.
DC   B03 B05
IN   ZELDIS, J B
PA   (ZELD-I) ZELDIS J B; (CELG-N) CELGENE CORP
CYC  110
PI   US--2005239867 A1 20051027 (200576)*      33    A61K-031-704
     WO--2005102317 A1 20051103 (200576)  EN         A61K-031-40
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            ZM ZW
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            DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
            KM KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO
            NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ
            UA UG US UZ VC VN YU ZA ZM ZW
ADT  US--2005239867 A1 Provisional 2004US-565174P 20040423, 2005US-0111187
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20050421; WO--2005102317 A1 2005WO-US13597 20050421
PRAI 2004US-565174P 20040423; 2005US-0111187 20050421
IC ICM A61K-031-40; A61K-031-704
ICS A61K-031-366; A61K-031-397; A61K-031-4035; A61K-031-519
AB US2005239867 A UPAB: 20051125
NOVELTY - Treatment, prevention, or managing pulmonary hypertension involves administration of phosphodiesterase-4 (PDE-4) modulator, its salt, solvate or stereoisomer.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a pharmaceutical composition comprising the PDE4 modulator, its salt, solvate or stereoisomer, and a second active agent capable of reducing pulmonary artery pressure or a symptom of pulmonary hypertension.
ACTIVITY - Hypotensive; Respiratory-Gen.; Cardiovascular-Gen.; Analgesic; Muscular-Gen.; Immunomodulator; Antiinflammatory; Cerebroprotective; Hypertensive; Anticonvulsant; Cardiant; CNS-Gen.
Efficacy of 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide (Ia) was evaluated in patients with pulmonary hypertension for 12 weeks. (Ia) Was administered at dosage of 1 - 1200 mg/day, and the patients were evaluated for decline in walk distance, dyspnea score, and pulmonary hemodynamic response. The patients treated with (Ia) showed improvement in dyspnea score as compared to placebo-treated patients (control). Also the patients treated with (Ia) walked approx. 70 meters farther after 12 weeks while the control group of the patients showed decline in walk distance; and there was decrease in pulmonary arterial pressure and pulmonary vascular resistance, and increase in cardiac output as compared to worsening of pulmonary hemodynamics in control group.
MECHANISM OF ACTION - PDE4 (phosphodiesterase) modulator; Selective cytokine inhibitor.
USE - For treating, prevention and managing primary and secondary pulmonary hypertension (e.g. of functional classes I - IV) before, during or after surgery or lung transplantation; and also for treating symptoms associated with pulmonary hypertension (claimed) including dyspnea, fatigue, weakness, chest pain, recurrent syncope, seizures, light-headedness, leg edema and palpitations.
ADVANTAGE - The PDE4 modulators are enantiomerically pure, and exhibit selective cytokine inhibitory activities (e.g. inhibit inflammatory cytokines such as tumor necrosis- alpha production in monocytes as well as in lymphocytes); exhibit excellent immunomodulatory activities that may provide additive or synergistic effect when given before, concurrently with, or after surgery or transplantation therapy; reduce complications associated with the transplantation as well as adverse side effects than the prior art therapies; improve exercise capacity; and provide safe and effective treatment and management therapy for pulmonary hypertension.
Dwg.0/0
FS CPI
FA AB; GI; DCN
MC CPI: B01-D02; B05-C03; B06-H; B07-H; B10-A17; B10-C03; B10-C04A; B10-E04A; B14-C01; B14-C03; B14-D07A1; B14-D07C; B14-E11; B14-F01A; B14-F02; B14-F04; B14-F06; B14-F07; B14-J01A2; B14-J05; B14-J07; B14-K01; B14-L01; B14-L04; B14-L06; B14-N08
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M2 *06* DCN: RA0WC2-M; RA0WC2-K
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M2 *10* DCN: RA0GH5-M; RA0GH5-K
M2 *11* DCN: RA00K2-M; RA00K2-K
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M2 *13* DCN: R01901-M; R01901-K
M2 *14* DCN: R04093-M; R04093-K; R04742-M; R04742-K

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M2 *23* DCN: RAK0AB-M; RAK0AB-U; RAK0AB-K
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M2 *25* DCN: RAK0AD-M; RAK0AD-U; RAK0AD-K
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M5 *18* DCN: R02018-M; R02018-K
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ABEX UPTX: 20051125
SPECIFIC COMPOUNDS - Use of 7 compounds as the PDE-4 modulator, e.g. 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide, cyclopropanecarboxylic acid (2-(1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl)-3-oxo-2,3-dihydro-1H-isoindol-4-yl-amide, and 4-(1-aza-2-(dimethylamino)prop-1-enyl)-2-(1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl)isoindoline-1,3-dione is specifically claimed.

ADMINISTRATION - Dosage of the PDE4 modulator is 1 - 10000 (preferably 1 - 2500, especially 1 - 20) mg/day; and that of the second agent is 1 - 1000 (preferably 50 - 200) mg. Administration is by oral, mucosal (e.g. nasal, sublingual, vaginal, buccal or rectal), or parenteral (e.g. subcutaneous, intravenous, intramuscular or intraarterial) route, or by inhalation.
TECH UPTX: 20051125
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The PDE4 modulator is a cyclic amide derivative of formula (I) or imido and amido substituted alkanohydroxamic acids of formula (II).
n=1 - 3;
R5=o-phenylene (optionally mono- -- tetra-substituted by nitro, cyano, trifluoromethyl, carboethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, 1-10C alkyl, or halo);
R7=phenyl (optionally substituted with at least one of T1), benzyl (optionally mono- - tri-substituted by T1), naphthyl, or benzyloxy;
T1=nitro, cyano, trifluoromethyl, carboethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, 1-10C alkyl, 1-10C alkoxy, or halo;
R12=OH, 1-12C alkoxy, or -NR8R9;
R8=H or 1-10C alkyl;
R9=H, 1-10C alkyl, COR10, or -SO2R10;
R10=H, 1-10C alkyl, or phenyl;
R1 and R2=H or lower alkyl;
CR1+CR2=o-phenylene, o-naphthylene, or cyclohexene-1,2-diyl (all optionally mono- - tetra-substituted by nitro, cyano, trifluoromethyl, carboethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, 1-10C alkyl, 1-10C alkoxy, or halo);
R3=phenyl (mono- - tetra-substituted by nitro, cyano, trifluoromethyl, carboethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, 1-10C alkyl, 1-10C alkoxy, 1-10C alkylthio, benzyloxy, 3-6C cycloalkoxy, 4-6C cycloalkylidenemethyl, 3-10C alkylidenemethyl, indanyloxy, or halo);
R4=H, 1-6C alkyl, phenyl, or benzyl;
R4a=H or 1-6C alkyl;
R5a=-CH2-, -CH2-CO-, -SO2-, -S-, or -NHCO-;
m=0 - 2.
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The method further involves administration of a second active agent that is capable of

reducing pulmonary artery pressure or symptoms of the pulmonary hypertension. Preferred Components: The second active agent is anticoagulant, diuretic, cardiac glycoside, calcium channel blocker, vasodilator, prostacyclin analogue, endothelin antagonist, phosphodiesterase inhibitor, endopeptidase inhibitor, lipid lowering agent, or a thromboxane inhibitor (preferably amlodipine, diltiazem, nifedipine, epoprostenol, treprostinil, bosentan, warfarin, tadalafil, simvastatin, omapatrilat, irbesartan, pravastatin, digoxin, nitric oxide, L-arginine, iloprost, betaprost, or sildenafil).

L42 ANSWER 2 OF 5 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2004-420074 [39] WPIX
CR 2004-034763 [03]; 2004-034766 [03]; 2004-420073 [39]; 2005-031046 [03]
DNC C2004-157704
TI Use of a cytokine inhibitory drug to treat, manage or prevent e.g. cancer and diseases associated with undesired **angiogenesis**.
DC B05
IN ZELDIS, J B
PA (CELG-N) CELGENE CORP; (ZELD-I) ZELDIS J B
CYC 108
PI WO--2004043378 A2 20040527 (200439)* EN 74 A61K-000-00
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
AU--2003290652 A1 20040603 (200470) A61K-000-00
EP-----1567154 A2 20050831 (200561) EN A61K-031-44
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
BR---200316057 A 20050920 (200566) A61K-031-44
US--2006035955 A1 20060216 (200613) A61K-031-403
JP--2006508131 W 20060309 (200620) 61 A61K-045-00
MX--2005004780 A1 20051001 (200620) A61K-031-40
KR--2005072802 A 20050712 (200643) A61K-031-44
ADT WO--2004043378 A2 2003WO-US035545 20031106; AU--2003290652 A1 2003AU-0290652 20031106; EP-----1567154 A2 2003EP-0783234 20031106, 2003WO-US35545 20031106; BR---200316057 A 2003BR-0016057 20031106, 2003WO-US35545 20031106; US--2006035955 A1 2003WO-US35545 20031106, 2005US-0534325 20050912; JP--2006508131 W 2003WO-US35545 20031106, 2004JP-0551873 20031106; MX--2005004780 A1 2003WO-US35545 20031106, 2005MX-0004780 20050504; KR--2005072802 A 2003WO-US35545 20031106, 2005KR-0708122 20050506
FDT AU--2003290652 A1 Based on WO--2004043378; EP-----1567154 A2 Based on WO--2004043378; BR---200316057 A Based on WO--2004043378; JP--2006508131 W Based on WO--2004043378; MX--2005004780 A1 Based on WO--2004043378; KR--2005072802 A Based on WO--2004043378
PRAI 2002US-424601P 20021106; 2005US-0534325 20050912
IC ICM A61K-000-00; A61K-031-40; A61K-031-403; A61K-031-4035; A61K-031-44; A61K-045-00
ICS A61K-031-415; A61K-031-425; A61K-031-519; A61K-031-522; A61K-038-19; A61P-035-00; A61P-043-00
AB WO2004043378 A UPAB: 20060706
NOVELTY - Treatment, management or prevention of a specific cancer, comprises administration of a therapeutically or prophylactically effective amount of a selective cytokine inhibitory drug (I) or a salt, solvate or stereoisomer.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a method of treating, managing or preventing a disease associated with undesired **angiogenesis**, comprising administration of (I);
(2) a method for reducing or avoiding an adverse effect associated with radiation therapy, hormonal therapy, biological therapy or immunotherapy and with administration of a second active ingredient (IV) in a patient suffering from cancer, comprises administration of (I);

(3) a method of treating, preventing or managing a specific cancer that is refractory to conventional therapy, which comprises administering (I) or a salt, solvate or stereoisomer and (IV) and transplanting umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow in the patient;

(4) a pharmaceutical composition (A) comprising (I) or a salt, solvate or stereoisomer and (IV);

(5) a kit comprising a pharmaceutical composition (B) comprising (I) or a salt, solvate or stereoisomer and a pharmaceutical composition (C) comprising (IV); and

(6) a kit comprising (B) and umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow.

ACTIVITY - Cytostatic; Anti-HIV; Dermatological; Vasotropic; Antidiabetic; Ophthalmological; Immunosuppressive; Antiinflammatory; Antiseborrheic; Antibacterial; Antilipemic; Antiulcer; Fungicide; Virucide; Auditory; Protozoacide; Antiarthritic; Antirheumatic; Tranquilizer; Vulnerary; Antianemic; Antisickling; Osteopathic; Cardiovascular-Gen.; CNS-Gen.; Gastrointestinal-Gen.; Cerebroprotective; **Antiangiogenic.**

MECHANISM OF ACTION - Cytokine inhibitor. Test details are described for cytokine inhibitory activity but no results given.

USE - (I) are useful for reducing or avoiding an adverse effect associated with the administration of (IV) and for treating, managing or preventing a specific cancer or a cancer that is refractory to conventional therapy (advanced malignancy, amyloidosis, neuroblastoma, meningioma, hemangiopericytoma, multiple brain metastase, glioblastoma multiforms, glioblastoma, brain stem glioma, poor prognosis malignant brain tumor, malignant glioma, anaplastic astrocytoma, anaplastic oligodendroglioma, neuroendocrine tumor, rectal adenocarcinoma, Dukes C and D colorectal cancer, unresectable colorectal carcinoma, metastatic hepatocellular carcinoma, Kaposi's sarcoma, karotype acute myeloblastic leukemia, Hodgkin's lymphoma, non-Hodgkin's lymphoma, cutaneous T-Cell lymphoma, cutaneous B-Cell lymphoma, diffuse large B-Cell lymphoma, low grade follicular lymphoma, metastatic melanoma, localized melanoma, malignant mesothelioma, malignant pleural effusion mesothelioma syndrome, peritoneal carcinoma, papillary serous carcinoma, gynecologic sarcoma, soft tissue sarcoma, scleroderma, cutaneous vasculitis, Langerhans cell histiocytosis, leiomyosarcoma, fibrodysplasia ossificans progressive, hormone refractory prostate cancer, resected high-risk soft tissue sarcoma, unrescectable hepatocellular carcinoma, Waldenstrom's macroglobulinemia, smoldering myeloma, indolent myeloma, fallopian tube cancer, androgen independent prostate cancer, androgen dependent stage IV non-metastatic prostate cancer, hormone-insensitive prostate cancer, chemotherapy-insensitive prostate cancer, papillary thyroid carcinoma, follicular thyroid carcinoma, medullary thyroid carcinoma or leiomyoma) and a disease (diabetic retinopathy, retinopathy of prematurity, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, proliferative vitreoretinopathy, trachoma, myopia, optic pits, epidemic keratoconjunctivitis, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, sjogrens, acne rosacea, phylectenulosis, syphilis, lipid degeneration, bacterial ulcer, fungal ulcer, Herpes simplex infection, Herpes zoster infection, protozoan infection, Mooren ulcer, Terrien's marginal degeneration, mariginal keratolysis, rheumatoid arthritis, systemic lupus, polyarteritis, trauma, Wegeners sarcoidosis, Scleritis, Steven's Johnson disease, periphigoid radial keratotomy, sickle cell anemia, sarcoid, pseudoxanthoma elasticum, Paget's disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis, chronic vitritis, Lyme's disease, Eales disease, Bechet's disease, retinitis, choroiditis, presumed ocular histoplasmosis, Bests disease, Stargarts disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, sclerosing cholangitis, rubeosis, endotoxemia, toxic shock syndrome, osteoarthritis, retrovirus replication, wasting, meningitis, silica-induced fibrosis, asbestos-induced fibrosis, veterinary disorder, malignancy-associated hypercalcemia, stroke, circulatory shock, periodontitis, gingivitis, macrocytic anemia,

refractory anemia or 5q-syndrome) associated with undesired angiogenesis (all claimed).
ADVANTAGE - (I) reduces adverse side effects.
Dwg.0/0

FS CPI
FA AB; GI; DCN
MC CPI: B01-B02; B02-D; B03-A; B04-A06; B04-B03A; B04-B03C; B04-B04D; B04-B04E; B04-F02; B04-H02B; B04-H04A; B04-H04C; B04-H05; B04-N06; B06-H; B07-H; B10-B01B; B14-A01; B14-A02; B14-A03; B14-A04; B14-C03; B14-C09; B14-F02B2; B14-F02D; **B14-F02F2**; B14-F03; B14-G02A; B14-G02C; B14-G02D; B14-H01; B14-J05B; B14-K01; B14-N03; B14-N06B; B14-N16; B14-N17; B14-P03; B14-S06
M1 *05* DCN: RAEG82-K; RAEG82-T; RAEG82-M
M1 *06* DCN: RA09LI-K; RA09LI-T; RA09LI-M; RA0O3V-K; RA0O3V-T; RA0O3V-M
M1 *07* DCN: RA0DNM-K; RA0DNM-T; RA0DNM-M; RA0KDA-K; RA0KDA-T; RA0KDA-M
M1 *08* DCN: RA02UP-K; RA02UP-T; RA02UP-M
M1 *09* DCN: R06364-K; R06364-T; R06364-M; R16207-K; R16207-T; R16207-M
M1 *10* DCN: RA022K-K; RA022K-T; RA022K-M
M2 *01* DCN: RA4TIW-K; RA4TIW-T; RA4TIW-M; RA4TIW-U
M2 *02* DCN: **RACI5Z-K; RACI5Z-T; RACI5Z-M; RACI5Z-U**
M2 *03* DCN: 0132-51801-K; 0132-51801-T; 0132-51801-M; 0132-51801-U
M2 *04* DCN: 0132-51802-K; 0132-51802-T; 0132-51802-M; 0132-51802-U
M2 *11* DCN: R01166-K; R01166-T; R01166-M
M2 *12* DCN: RA035F-K; RA035F-T; RA035F-M; RA2PVY-K; RA2PVY-T; RA2PVY-M
M2 *13* DCN: R10440-K; R10440-T; R10440-M
M2 *14* DCN: RA01E9-K; RA01E9-T; RA01E9-M
M2 *15* DCN: RA035H-K; RA035H-T; RA035H-M
M2 *16* DCN: R10124-K; R10124-T; R10124-M
M2 *17* DCN: R02028-K; R02028-T; R02028-M; R08024-K; R08024-T; R08024-M
M2 *18* DCN: R00125-K; R00125-T; R00125-M; R17770-K; R17770-T; R17770-M
M2 *19* DCN: R08225-K; R08225-T; R08225-M
M2 *20* DCN: RA021Q-K; RA021Q-T; RA021Q-M
M2 *21* DCN: R17804-K; R17804-T; R17804-M
M2 *22* DCN: R07202-K; R07202-T; R07202-M
M5 *23* DCN: R00002-K; R00002-T; R00002-M; R14648-K; R14648-T; R14648-M
DCRE 433262-0-0-0; 817201-0-0-0; 869582-0-0-0; 91489-0-0-0; 114126-0-0-0; 94444-0-0-0; 97946-0-0-0; 97854-0-0-0; 106545-2-0-0; 109181-1-0-0; 14620-0-0-0; 93613-1-0-0; 98147-1-0-0; 91082-0-0-0; 8769-1-0-0; 110156-1-0-0; 92243-0-0-0; 8220-2-0-0; 133806-1-0-0; 10897-0-0-0; 88752-2-0-0
ABEX UPTX: 20040621
SPECIFIC COMPOUNDS - The use of 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide and cyclopropanecarboxylic acid (2-(1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl)-3-oxo-2,3-dihydro-1H-isoindol-4-yl-amide is specifically claimed as (I).

ADMINISTRATION - Administration of (I) is 1-10000 mg/day (claimed), orally, mucosally, parenterally, topically, transdermally or transcutaneously.
TECH UPTX: 20040621
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The treatment of cancer further comprises administration of a second active ingredient, radiation therapy, hormonal therapy, biological therapy or immunotherapy. The disease associated with undesired angiogenesis further comprises administering a second active ingredient (IV). (IV) is hematopoietic growth factor, cytokine, anti-cancer agent, antibiotic, cyclooxygenase (COX)-2 inhibitor, immunomodulatory agent, immunosuppressive agent, corticosteroid or a pharmacologically active mutant or derivative or a combination (preferably oblimersen, melphalan, granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage (GM)-CSF, EPO (preferably Epogen (RTM; epoetin alpha)), topotecan, pentoxifylline, taxotere, irinotecan, COX-2 inhibitor, ciprofloxacin, dexamethasone, doxorubicin, vincristine, interleukin (IL)-2, interferon (IFN), dacarbazine, Ara-C, vinorelbine, isotretinoin or a salt, solvate or stereoisomer or a pharmacologically active mutant or derivative or a

combination). (I) is an azetidine derivative of formula (II) or pyrrol-2-one derivative of formula (III). (I) is administered before, during or after surgery directed at relieving, reducing or avoiding a symptom of a specific cancer in the patient. (IV) is administered prior to, during or after transplanting umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow in the patient. (I) is administered prior to, during or after the administration of (IV), radiation therapy, hormonal therapy, biological therapy or immunotherapy. (I), (II) and (III) are enantiomerically pure.
n = 1-3;
R5 = o-phenylene (optionally substituted with 1-4 substituents of T);
T = nitro, CN, CF3, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, OH, amino, alkylamino, dialkylamino, acylamino, 1-10C alkyl or halo;
R7 = phenyl (optionally substituted with one or more of Ta), benzyl (optionally substituted with 1-3 of Ta), naphthyl or benzyloxy;
Ta = nitro, CN, CF3, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, OH, amino, 1-10C alkyl, 1-10C alkoxy or halo;
R12 = OH, 1-12C alkoxy or -N(R8R9);
R8 = H or 1-10C alkyl;
R9 = R8, COR10 or SO2R10; and
R10 = R8 or phenyl;
R1, R2 = H or lower alkyl; or
CR1R2 = o-phenylene, o-naphthylene, or cyclohexene-1,2-diyl (optionally substituted with 1-4 substituents of T');
T' = nitro, CN, CF3, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, OH, amino, alkylamino, dialkylamino, acylamino, 1-10C alkyl, 1-10C alkoxy or halo);
R3 = phenyl substituted with 1-4 substituents of T, 1-10C alkylthio, benzyloxy, 3-6C cycloalkoxy, 4-6C-cycloalkylidenemethyl, 3-10C -alkylidenemethyl or indanyloxy;
R4 = H, 1-6C alkyl, phenyl or benzyl;
R4' = H or 1-6C alkyl;
R5' = CH2, CH2-CO, SO2, S or NHCO; and
n' = 0-2.

L42 ANSWER 3 OF 5 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2004-388904 [36] WPIX
DNC C2004-145546
TI Use of selective cytokine inhibitory drugs, for treating, preventing or managing macular degeneration, e.g. wet or dry macular degeneration, age-related maculopathy, Best's disease, fundus flavimaculatus, or vitelliform.
DC B04 B05 D16
IN ZELDIS, J B
PA (ZELD-I) ZELDIS J B; (CELG-N) CELGENE CORP
CYC 110
PI US--2004091454 A1 20040513 (200436)* 19 A61K-038-21
WO--2004041181 A2 20040521 (200436) EN A61K-000-00
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
AU--2003285107 A1 20040607 (200469) A61K-038-21
WO--2005044269 A1 20050519 (200534) EN A61K-031-445
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
EP-----1567148 A2 20050831 (200561) EN A61K-031-40

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR

BR---200315889 A 20051004 (200566) A61K-031-40
TW---200418455 A 20041001 (200608) A61K-031-4035
JP--2006509743 W 20060323 (200623) 36 A61K-045-00
KR--2005062649 A 20050623 (200641) A61K-031-404
CN-----1731997 A 20060208 (200643) A61K-031-40

ADT US--2004091454 A1 Provisional 2002US-422900P 20021031, 2003US-0699110 20031030; WO--2004041181 A2 2003WO-US34535 20031031; AU--2003285107 A1 2003AU-0285107 20031031; WO--2005044269 A1 2004WO-US13253 20040428; EP-----1567148 A2 2003EP-0779423 20031031, 2003WO-US34535 20031031; BR---200315889 A 2003BR-0015889 20031031, 2003WO-US34535 20031031; TW---200418455 A 2003TW-0130486 20031031; JP--2006509743 W 2003WO-US34535 20031031, 2004JP-0550274 20031031; KR--2005062649 A 2003WO-US34535 20031031, 2005KR-0707608 20050429; CN-----1731997 A 2003CN-80108090 20031031

FDT AU--2003285107 A1 Based on WO--2004041181; EP-----1567148 A2 Based on WO--2004041181; BR---200315889 A Based on WO--2004041181; JP--2006509743 W Based on WO--2004041181; KR--2005062649 A Based on WO--2004041181

PRAI 2002US-422900P 20021031; 2003US-0699110 20031030

IC ICM A61K-000-00; A61K-031-40; A61K-031-4035; A61K-031-404; A61K-031-445; A61K-038-21; A61K-045-00

ICS A61K-031-00; A61K-031-403; A61K-031-409; A61K-031-4523; A61K-031-454; A61K-031-522; A61K-031-545; A61K-031-557; A61K-031-56; A61K-039-395; A61K-045-06; **A61P-009-00**; **A61P-009-10**; A61P-027-00; A61P-027-02

AB US2004091454 A UPAB: 20040608

NOVELTY - A method of treating, preventing or managing macular degeneration comprises administering to a patient a selective cytokine inhibitory drug, or its pharmaceutical salt, solvate, or stereoisomer.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a pharmaceutical composition comprising a selective cytokine inhibitory drug, or its pharmaceutical salt, solvate, or stereoisomer, and a second active agent capable of reducing or avoiding a symptom of macular degeneration.

ACTIVITY - Ophthalmological.

No biological data given.

MECHANISM OF ACTION - Cytokine inhibitor.

USE - The method is useful for treating, preventing or managing macular degeneration, such as wet macular degeneration, dry macular degeneration, age-related macular degeneration, age-related maculopathy, choroidal neovascularization, retinal pigment epithelium detachment, atrophy of retinal pigment epithelium, Best's disease, vitelliform, Stargardt's disease, juvenile macular dystrophy, fundus flavimaculatus, Behr's disease, Sorsby's disease, Doyne's disease, honeycomb dystrophy, or macular damaging condition (claimed).

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B04-A06; B04-G02; B04-H03; B04-H05; B04-H21; B04-J02; B04-J05; B05-A02; B06-H; B07-H; **B14-F02F2**; B14-L05; B14-N03; D05-H11

M1 *08* DCN: RA1PSH-K; RA1PSH-M
M1 *09* DCN: RA022K-K; RA022K-M
M1 *10* DCN: RA078O-K; RA078O-M
M1 *11* DCN: RA00F4-K; RA00F4-M
M1 *12* DCN: RA0WK5-K; RA0WK5-M
M1 *13* DCN: RA0WK5-K; RA0WK5-M
M2 *01* DCN: RA4TIW-K; RA4TIW-T; RA4TIW-M; RA4TIW-U
M2 *02* DCN: RAE95F-K; RAE95F-T; RAE95F-M; RAE95F-U
M2 *03* DCN: RAE95E-K; RAE95E-T; RAE95E-M; RAE95E-U
M2 *04* DCN: **RACI5Z-K**; **RACI5Z-T**; **RACI5Z-M**; **RACI5Z-U**
M2 *05* DCN: 0131-62201-K; 0131-62201-T; 0131-62201-M; 0131-62201-U
M2 *06* DCN: 0131-62202-K; 0131-62202-T; 0131-62202-M; 0131-62202-U
M2 *07* DCN: 0131-62203-K; 0131-62203-T; 0131-62203-M; 0131-62203-U
M2 *14* DCN: R23692-K; R23692-T; R23692-M

M2 *15* DCN: RA1QSX-K; RA1QSX-M
M2 *16* DCN: R10440-K; R10440-M
M2 *17* DCN: RA1ZZX-K; RA1ZZX-M
DCRE 433262-0-0-0; 433262-2-0-0; 433262-1-0-0; 817201-0-0-0; 282324-0-0-0; 97854-0-0-0; 107425-0-0-0; 107436-0-0-0; 97861-0-0-0; 108692-0-0-0; 88666-1-0-0; 14620-0-0-0; 94674-0-0-0; 97861-0-0-0
ABEX UPTX: 20040608
WIDER DISCLOSURE - Also disclosed is a kit comprising the pharmaceutical composition, and additional active agents.

ADMINISTRATION - The selective cytokine inhibitory drug is administered at a dose of 1-10000 mg. Administration can be parenteral (e.g. intravitreal, intravenous, intramuscular, or intraarterial), oral, topical or mucosal.
TECH UPTX: 20040608
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The method further comprises administering a second active agent selected from a steroid, a light sensitizer, an integrin, an antioxidant, an interferon, a xanthine derivative, a growth hormone, a neutrotrophic factor, a regulator of neovascularization, an anti-vascular endothelial growth factor (VEGF) antibody, a prostaglandin, an antibiotic, a phytoestrogen, an anti-inflammatory compound, an **antiangiogenesis** compound (such as thalidomide), thalidomide, verteporfin, purlytin, an angiostatic steroid, rhuFab, interferon-2alpha, pentoxifylline, or its pharmaceutical salt, solvate, or stereoisomer.
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Drug: The selective cytokine inhibitory drug is stereomerically pure. Specifically, the method comprises administering 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide, cyclopropanecarboxylic acid (2-(1(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl)-3-oxo-2,3-dihydro-1H-isoindol-4-yl-amide, or their pharmaceutical salt, solvate, or stereoisomer, where the compounds are enantiomerically pure. The selective cytokine inhibitory drug is formula (I), (II) or (III).
For (I),
n = 1-3;
R5 = o-phenylene, unsubstituted or substituted with 1-4 substituents each selected independently from nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, 1-10C alkyl, 1-10C, and halo;
R7 = phenyl or phenyl substituted with one or more substituents each selected independently from nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1-10 carbon atoms, alkoxy of 1-0 carbon atoms, and halo; benzyl unsubstituted or substituted with 1-3 substituents selected from nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, 1-10C alkyl, 1-10C alkoxy and halo; naphthyl, or benzyloxy;
R12 = -OH, 1-12C alkoxy, or (Ia);
R8 = hydrogen or 1-10C alkyl;
R9 = hydrogen, 1-10C alkyl, -COR10, or -SO2R10; and
R10 = hydrogen, 1-10C alkyl, or phenyl
For (II),
R1 and R2 = when taken independently of each other, is hydrogen, lower alkyl, or R1 and R2, when taken together with the depicted carbon atoms to which each is bound, is o-phenylene, o-naphthylene, or cyclohexene-1,2-diyl, unsubstituted or substituted with 1-4 substituents each selected independently from nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, 1-10C alkyl, 1-10C alkoxy, and halo;
R3 = phenyl substituted with from 1-4 substituents selected from nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, 1-10C alkyl, 1-10C alkoxy, 1-10C alkylthio, benzyloxy, 3-6C cycloalkoxy, 4-6C cycloalkylidenemethyl, 3-10C alkylidenemethyl, indanyloxy, and halo;
R4 = hydrogen, alkyl of 1-6 carbon atoms, phenyl, or benzyl;
R4' = H or 1-6C alkyl

R5 = -CH2-, -CH2-CO, -SO2-, -S-, or -NHCO-; and
n = 0, 1, or 2
For (II),
Y = C=O, CH2, SO2, or CH2C=O;
R1, R2, R3, and R4 = independently selected from hydrogen, halo, 1-2C, 1-4C alkoxy, nitro, cyano, hydroxy, or -NR8R9; or any 2 of R1, R2, R3, and R4 on adjacent carbon atoms, together with the depicted phenylene ring are naphthylidene;
R5 and R6 = independently of the other, is hydrogen, 1-4C alkyl, 1-4C alkoxy, cyano, or cycloalkoxy of up to 18 carbon atoms;
R7 = hydroxy, alkyl of 1-8 carbon atoms, phenyl, benzyl, or NR8R9;
R8 and R9 = taken independently of the other is hydrogen, 1-8C alkyl, phenyl, or benzyl; R8 or R9 is hydrogen and the other is -COR10 or -SO2R10; or R8 and R9 taken together are tetramethylene, pentamethylene, hexamethylene, or -CH2CH2X1CH2CH2- in which X1 is -O-, -S-, or -NH-; and R8' and R9' = taken independently of the other is hydrogen, alkyl of 1-8 carbon atoms, phenyl, or benzyl; R8' or R9' = hydrogen and the other is -CO10'- or -SO2R10'; or R8' and R9' = taken together are tetramethylene, pentamethylene, hexamethylene, or -CH2CH2X2CH2CH2- in which X2 -O-, -S-, or -NH-.
The selective cytokine inhibitory drug, or its salt, solvate, or stereoisomer may be administered before, during or after surgical intervention directed at reducing or avoiding a symptom of macular degeneration in the patient. The surgical intervention may be light therapy, laser therapy, radiation therapy, retinal pigment epithelium transplantation, or foveal translocation.

L42 ANSWER 4 OF 5 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2004-365426 [34] WPIX
DNC C2004-137967
TI Use of a selective cytokine inhibitory drug in the treatment, prevention, modification or management of pain e.g. visceral pain, migraine, tension type headache or post-operative pain.
DC B05
IN FALECK, H; MANNING, D C; ZELDIS, J B
PA (FALE-I) FALECK H; (MANN-I) MANNING D C; (ZELD-I) ZELDIS J B; (CELG-N) CELGENE CORP
CYC 108
PI WO--2004037207 A2 20040506 (200434)* EN 62 A61K-000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
US--2004087558 A1 20040506 (200434) A61K-031-60
AU--2003284979 A1 20040513 (200468) A61K-000-00
EP-----1562586 A2 20050817 (200554) EN A61K-031-405
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
BR---200315593 A 20050906 (200560) A61K-031-405
TW---200412943 A 20040801 (200581) A61K-031-395
JP--2006505591 W 20060216 (200614) 48 A61K-045-00
CN-----1731998 A 20060208 (200643) A61K-031-403
KR--2005072113 A 20050708 (200643) A61K-031-405
ADT WO--2004037207 A2 2003WO-US034005 20031024; US--2004087558 A1 Provisional 2002US-421004P 20021024, 2003US-0693722 20031023; AU--2003284979 A1 2003AU-0284979 20031024; EP-----1562586 A2 2003EP-0779299 20031024, 2003WO-US34005 20031024; BR---200315593 A 2003BR-0015593 20031024, 2003WO-US34005 20031024; TW---200412943 A 2003TW-0129607 20031024; JP--2006505591 W 2003WO-US34005 20031024, 2004JP-0547196 20031024; CN-----1731998 A 2003CN-80107547 20031024; KR--2005072113 A 2003WO-US34005 20031024, 2005KR-0707018 20050422
FDT AU--2003284979 A1 Based on WO--2004037207; EP-----1562586 A2 Based on WO--2004037207; BR---200315593 A Based on WO--2004037207; JP--2006505591 W

Based on WO--2004037207; KR--2005072113 A Based on WO--2004037207
PRAI 2002US-421004P 20021024; 2003US-0693722 20031023
IC ICM A61K-000-00; A61K-031-395; A61K-031-403; A61K-031-405; A61K-031-60; A61K-045-00
ICS A61K-031-095; A61K-031-10; A61K-031-19; A61K-031-192; A61K-031-40; A61K-031-445; A61K-031-485; A61K-031-573; A61P-025-00; A61P-025-04; A61P-025-06; A61P-029-00; A61P-043-00
AB WO2004037207 A UPAB: 20040527
NOVELTY - Treatment, prevention, modification or management of pain comprises administration of a selective cytokine inhibitory drug (I) or its salt, solvate or stereoisomer.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a composition comprising (I) or its salt, solvate or stereoisomer and (II), capable of relieving or reducing pain.

ACTIVITY - Analgesic; Antimigraine.

MECHANISM OF ACTION - Selective cytokine inhibitor.

USE - (I) is useful in the treatment, prevention, modification or management of pain (nociceptive pain and/or neuropathic pain, visceral pain, migraine, tension type headache or post-operative pain) associated with chemical/thermal burn, cut of the skin, contusion of the skin, osteoarthritis, rheumatoid arthritis, tendonitis or myofascial pain (particularly diabetic neuropathy, post herpetic neuralgia, trigeminal neuralgia, post-stroke pain, complex regional pain syndrome (type I or II), sympathetic maintained pain syndrome, reflex sympathetic dystrophy, reflex neurovascular dystrophy, reflex dystrophy, spinal cord injury pain, Sudeck atrophy of bone, algoneurodystrophy, shoulder hand syndrome, post-traumatic dystrophy, cancer related pain, phantom limb pain, fibromyalgia, chronic fatigue syndrome, radiculopathy, luetic neuropathy or painful neuropathic condition induced from a drug (iatrogenically induced by vincristine, velcade or thalidomide)) (claimed).

The biological effectiveness of compounds (I) (3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide) were tested in patients with pain syndromes for three to six months. The results showed that (I) have analgesic benefit in this disease.

Dwg.0/0
FS CPI
FA AB; GI; DCN
MC CPI: B01-B01; B04-A04; B06-A01; B06-A03; B06-D01; B06-D03; B06-D09; B06-D12; B06-E05; B07-D04D; B07-D05; B07-D08; B07-D09; B10-B02E; B10-B04B; B10-C03; B10-C04C; B10-C04E; B10-D03; B14-A01; B14-A04; B14-C01; B14-C03; B14-C07; B14-D05C; B14-F01; B14-F02B; B14-G02; B14-G03; B14-J01A1; B14-J01B4; B14-J02C1; B14-J02D1; B14-J05A; B14-J07; B14-L06
M2 *01* DCN: RA4TIW-K; RA4TIW-T; RA4TIW-M; RA4TIW-U
M2 *02* DCN: **RACI5Z-K; RACI5Z-T; RACI5Z-M; RACI5Z-U**
M2 *03* DCN: 0130-78501-K; 0130-78501-T; 0130-78501-M; 0130-78501-U
M2 *04* DCN: 0130-78502-K; 0130-78502-T; 0130-78502-M; 0130-78502-U
M2 *05* DCN: 0130-78503-K; 0130-78503-T; 0130-78503-M; 0130-78503-U
M2 *06* DCN: 0130-78504-K; 0130-78504-T; 0130-78504-M; 0130-78504-U
M2 *07* DCN: 0130-78505-K; 0130-78505-T; 0130-78505-M; 0130-78505-U
M2 *08* DCN: R00034-K; R00034-T; R00034-M; R06663-K; R06663-T; R06663-M
M2 *09* DCN: RA027G-K; RA027G-T; RA027G-M
M2 *10* DCN: R01651-K; R01651-T; R01651-M
M2 *11* DCN: R18780-K; R18780-T; R18780-M
M2 *12* DCN: R01203-K; R01203-T; R01203-M
M2 *13* DCN: R21564-K; R21564-T; R21564-M
M2 *14* DCN: R00129-K; R00129-T; R00129-M; R04339-K; R04339-T; R04339-M
M2 *15* DCN: R03911-K; R03911-T; R03911-M
M2 *16* DCN: R03027-K; R03027-T; R03027-M; R11668-K; R11668-T; R11668-M
M2 *17* DCN: R01627-K; R01627-T; R01627-M; R06674-K; R06674-T; R06674-M
M2 *18* DCN: R06854-K; R06854-T; R06854-M; R16303-K; R16303-T; R16303-M
M2 *19* DCN: R00130-K; R00130-T; R00130-M; R16302-K; R16302-T; R16302-M
M2 *20* DCN: R07434-K; R07434-T; R07434-M
M2 *21* DCN: R03169-K; R03169-T; R03169-M; R10726-K; R10726-T; R10726-M
M2 *22* DCN: R01254-K; R01254-T; R01254-M; R16301-K; R16301-T; R16301-M

M2 *23* DCN: R00758-K; R00758-T; R00758-M; R16282-K; R16282-T; R16282-M
M2 *24* DCN: R01987-K; R01987-T; R01987-M; R06547-K; R06547-T; R06547-M; R11757-K; R11757-T; R11757-M; R14131-K; R14131-T; R14131-M
M2 *25* DCN: RA01BE-K; RA01BE-T; RA01BE-M
M2 *26* DCN: R01073-K; R01073-T; R01073-M
M2 *27* DCN: R00022-K; R00022-T; R00022-M; R16160-K; R16160-T; R16160-M
M2 *28* DCN: R00023-K; R00023-T; R00023-M; R11478-K; R11478-T; R11478-M
M2 *29* DCN: R07411-K; R07411-T; R07411-M; R16161-K; R16161-T; R16161-M
M5 *30* DCN: R00067-K; R00067-T; R00067-M
DCRE 433262-0-0-0; 817201-0-0-0; 87874-0-0-0; 127393-0-0-0; 61643-0-0-0; 95795-0-0-0; 44063-0-0-0; 102950-0-0-0; 77147-0-0-0; 110010-0-4-0; 6754-0-0-0; 91319-0-0-0; 103043-1-0-0; 13312-0-0-0; 148654-1-0-0; 97160-1-0-0; 95048-0-0-0; 5735-0-0-0; 7556-0-0-0; 72366-0-1-0; 35431-1-0-0; 87308-0-0-0; 97730-0-0-0; 93683-0-0-0; 104629-1-0-0
ABEX UPTX: 20040527
SPECIFIC COMPOUNDS - The use of salicylic acid acetate, celecoxib, ketamine, gabapentin, carbamazepine, oxcarbazepine, phenytoin, sodium valproate, prednisone, nifedipine, clonidine, oxycodone, meperidine, morphine sulfate, hydromorphone, fentanyl, acetaminophen, ibuprofen, naproxen sodium, griseofulvin, amitriptyline, imipramine and doxepin is specifically claimed as (II). The use of 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide and cyclopropanecarboxylic acid (2-(1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonylethyl)-3-oxo-2,3 -dihydro-1H-isoindol-4-yl) -amide is specifically claimed as (I).

ADMINISTRATION - Administration of (I) is 1-10,000 (preferably 100-800) mg/day, orally. Administration of (II) is 1-3,500 (preferably 25-250) mg/day, orally, intravenously, intramuscularly, subcutaneously, mucosally, or transdermally.
TECH UPTX: 20040527
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Process: The method further comprises the administration of at least one second active agent (II) that is capable of relieving or reducing pain. (I) is administered before, during or after surgery, psychological or physical therapy directed at reducing or avoiding a symptom of pain in the patient.
Preferred Components: (II) is an antidepressant, antihypertensive agent, anxiolytic agent, calcium channel blocker, alpha-adrenergic receptor agonist, alpha-adrenergic receptor antagonist, ketamine, anesthetic, muscle relaxant, non-narcotic analgesic, opioid analgesic, anti-inflammatory agent, immunomodulatory agent, immunosuppressive agent, corticosteroid, anticonvulsant, cyclooxygenase-2 inhibitor and/or hyperbaric oxygen. The stereoisomers of (I) are enantiomerically pure. (I) is preferably a carbonyl compound of formulae (1), (2) or (3).
R5 = o-phenylene (optionally substituted with 1-4 of (di)alkylamino, acylamino or T);
R7 = phenyl (optionally substituted with T), benzyl (optionally substituted with 1-3 of T), naphthyl or benzyloxy;
R12 = OH, 1-12C alkoxy or N(R8)R9;
R8 = H or 1-10C alkyl; and
R9 = H, 1-10C alkyl, COR10 or SO2R10;
R10 = H, 1-10C alkyl or phenyl;
T = NO2, CN, CF3, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, COOH, OH, NH2, 1-10C alkyl, 1-10C alkoxy or halo; and
n = 1-3.
Either R1, R2 = H or lower alkyl; or
CR1R2 = o-phenylene, o-naphthylene or cyclohexene-1,2-diyl (optionally substituted with 1-4 of (di)alkylamino, acylamino or T);
R3 = phenyl (substituted with 1-4 of NO2, CN, CF3, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, COOH, OH, NH2, 1-10C alkyl, 1-10C alkoxy, 1-10C alkylthio, benzyloxy, 3-6C cycloalkoxy, 4-6C cycloalkylidenemethyl, 3-10C alkylidenemethyl, indanyloxy or halo);
R4 = H, 1-6C alkyl, phenyl or benzyl;
R4 = H or 1-6C alkyl;
R5 = CH2, CH2-CO, SO2, S or NHCO; and
n = 0-2.
Y' = C-O, CH2, SO2 or CH2C-O;

asterisk = center of chirality;
R1-R4 = H, halo, 1-4C alkyl, 1-4C alkoxy, NO2, CN, OH or NR8R9; or
any two of R1, R2, R3 or R4 (on adjacent carbon atoms together with
phenylene) = naphthylidene;
R5, R6 = H, 1-4C alkyl, 1-4C alkoxy, CN or 1-18C cycloalkoxy;
R7 = OH, 1-8 alkyl, phenyl, benzyl or NR8 R9;
either R8, R9 = H, 1-8C alkyl, phenyl or benzyl; or
R8R9 = tetramethylene, pentamethylene, hexamethylene or CH2CH2X1CH2CH2; or
either R8 = H; and
R9 = COR10 or SO2R10; or vice versa;
X1 = O, S or NH;
either R8', R9' = H, 1-8C alkyl, phenyl or benzyl; or
R8'R9' = tetramethylene, pentamethylene, hexamethylene or CH2CH2X2CH2CH2;
or
either R8' = H; and
R9' = COR10' or SO2R10'; or vice versa; and
X2 = O, S or NH.

L42 ANSWER 5 OF 5 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2004-034763 [03] WPIX
CR 2004-034766 [03]; 2004-420073 [39]; 2004-420074 [39]; 2005-031046 [03]
DNC C2004-011468
TI Use of selective cytokine inhibitory drug e.g. 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide to treat cancers and diseases associated with undesired **angiogenesis**.
DC B03
IN ZELDIS, J B
PA (CELG-N) CELGENE CORP; (BARE-I) BARER S J
CYC 109
PI WO--2003097040 A1 20031127 (200403)* EN 62 A61K-031-40
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
AU--2003234624 A1 20031202 (200442) A61K-031-40
KR--2005010812 A 20050128 (200535) A61K-031-445
EP-----1556033 A1 20050727 (200549) EN A61K-031-40
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
JP--2005530780 W 20051013 (200568) 49 A61K-045-00
MX--2004011310 A1 20050301 (200568) A61K-031-40
US--2005234017 A1 20051020 (200569) A61K-031-724
WO--2005112918 A1 20051201 (200580)# EN A61K-031-40
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
CN-----1668296 A 20050914 (200607) A61K-031-40
CN-----1697655 A 20051116 (200620) A61K-031-445
CN-----1735412 A 20060215 (200643) A61K-031-44
ADT WO--2003097040 A1 2003WO-US015468 20030516; AU--2003234624 A1 2003AU-0234624 20030516; KR--2005010812 A 2004KR-0718550 20041117; EP-----1556033 A1 2003EP-0728967 20030516, 2003WO-US15468 20030516; JP--2005530780 W 2003WO-US15468 20030516, 2004JP-0505039 20030516; MX--2004011310 A1 2003WO-US15468 20030516, 2004MX-0011310 20041115; US--2005234017 A1 2003WO-US15468 20030516, 2005US-0515270 20050523; WO--2005112918 A1 2004WO-US14002 20040505; CN-----1668296 A 2003CN-0816968 20030516; CN-----1697655 A 2003CN-0816899 20030516; CN-----1735412 A 2003CN-80108390 20031106
FDT AU--2003234624 A1 Based on WO--2003097040; EP-----1556033 A1 Based on

WO--2003097040; JP--2005530780 W Based on WO--2003097040; MX--2004011310 A1 Based on WO--2003097040

PRAI 2002US-424601P 20021106; 2002US-380842P 20020517; 2004WO-US014002 20040505; 2002US-424600P 20021106

IC ICM A61K-031-40; A61K-031-44; A61K-031-445; A61K-031-724; A61K-045-00
ICS A61K-031-198; A61K-031-4035; A61K-031-415; A61K-031-425; A61K-031-496; A61K-031-515; A61K-031-573; A61K-031-704; A61K-038-18; A61K-038-20; A61K-045-06; A61P-001-04; A61P-001-16; A61P-003-06; A61P-007-02; A61P-007-06; **A61P-009-04**; **A61P-009-10** ; **A61P-009-14**; A61P-011-00; A61P-011-06; A61P-011-16; A61P-017-02; A61P-017-06; A61P-017-10; A61P-019-02; A61P-019-08; A61P-025-00; A61P-027-02; A61P-027-06; A61P-027-10; A61P-027-14; A61P-029-00; A61P-031-00; A61P-031-04; A61P-031-10; A61P-031-12; A61P-031-18; A61P-033-00; A61P-033-02; A61P-033-06; A61P-035-00; A61P-035-02; A61P-035-04; A61P-037-00; A61P-037-06; A61P-037-08; A61P-041-00; A61P-043-00; C07D-401-00

AB WO2003097040 A UPAB: 20060706

NOVELTY - Treating, managing or preventing a specific cancer or disease associated with undesired **angiogenesis** comprises selective cytokine inhibitory drug and their salts, solvates, hydrates, stereoisomers, clathrates or prodrugs.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) composition comprising a selective cytokine inhibitory drug and their salts, solvates, hydrates, stereoisomers, clathrates or prodrugs and a second active ingredient (A); and

(2) a kit comprising a selective cytokine inhibitor drug and second active ingredient (chosen from hematopoietic growth factor, cytokine, anticancer agents, antibiotic, a cyclooxygenase-2 inhibitor, immunomodulatory agent, immunosuppressive agent, corticosteroid or their mutants and/or derivatives) or umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow.

ACTIVITY - Cytostatic; **Antiangiogenic**; Antidiabetic; Ophthalmological; Immunosuppressive; Anti-HIV; Antiseborrheic; Dermatological; Antibacterial; Antiulcer; Virucide; Auditory; Protozoacide; Antiarthritic; Antirheumatic; Antiinflammatory; Vulnerary; Antianemic.

Selective cytokine inhibitory drug was tested in patients with relapsed and refractory Dune-salmon stage III multiple myeloma. The results showed that the therapy comprising selective cytokine inhibitory drug in combination with melphalan and dexamethasone was highly active and generally tolerated in heavily pretreated multiple myeloma patients whose prognosis was otherwise poor.

MECHANISM OF ACTION - Cytokine production inhibitor; Tumor necrosis factor-alpha inhibitor.

USE - The selective cytokine inhibitory drug is useful in the treatment of specific cancer (preferably advanced malignancy, amyloidosis, locally advanced bladder cancer, metastatic transitional cell bladder cancer, relapsed brain tumor, progressive brain tumor, neuroblastoma, meningioma, hemangiopericytoma, multiple brain metastase, glioblastoma multiforms, glioblastoma, brain stem glioma, poor prognosis malignant brain tumor, malignant glioma, anaplastic astrocytoma, anaplastic oligodendroglioma, metastatic breast cancer, neuroendocrine tumor, rectal adenocarcinoma, Dukes C and D colorectal cancer, unrespectable colorectal carcinoma, metastatic hepatocellular carcinoma, Kaposi's sarcoma, karotype acute myeloblastic leukemia, Hodgkin's lymphoma, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, cutaneous B-Cell lymphoma, diffuse large B-Cell lymphoma, low grade follicular lymphoma, malignant melanoma, malignant mesothelioma, stage IIIB non-small cell lung cancer, malignant pleural effusion mesothelioma syndrome, multiple myeloma, peritoneal carcinoma, papillary serous carcinoma, gynecologic sarcoma, soft tissue sarcoma, scleroderma, cutaneous vasculitis, Langerhans cell histiocytosis, leiomyosarcoma, fibrodysplasia ossificans progressive, hormone refractory prostate cancer, resected high-risk soft tissue sarcoma, unresectable hepatocellular carcinoma, Waldenstrom's macroglobulinemia, smoldering myeloma, indolent myeloma, fallopian tube cancer, androgen independent

prostate cancer, androgen dependent stage IV non-metastatic prostate cancer, hormone-insensitive prostate cancer, chemotherapy-insensitive prostate cancer, papillary thyroid carcinoma, follicular thyroid carcinoma, medullary thyroid carcinoma or leiomyoma) and disease associated with undesired **angiogenesis** (preferably diabetic retinopathy, retinopathy of prematurity, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, proliferative vitreoretinopathy, trachoma, myopia, optic pits, epidemnic keratoconjunctivitis, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, Sjogren's, acne rosaceae, phylectenulosis, syphilis, lipid degeneration, bacterial ulcer, fungal ulcer, Herpes simplex infection, Herpes zoster infection, protozoan infection, Kaposi's sarcoma, Mooren ulcer, Terrine's marginal degeneration, marginal keratolysis, rheumatoid arthritis, systemic lupus, polyarteritis, trauma, Wegener's sarcoidosis, scleritis, Steven's Johnson disease, periphigoid radial keratotomy, sickle cell anemia, sarcoid, pseudoxanthoma elasticum, Paget's disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis, chronic vitritis, Lyme's disease, Eales disease, Behcet's disease, retinitis, thyroiditis, presumed ocular histoplasmosis, Bests disease, Stargarts disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, sclerosing cholangitis or rubeosis. The immunomodulatory compound is also useful in the reducing or avoiding an adverse effect associate with the administration of second active ingredient, radiation therapy, hormonal therapy, biological therapy or immuno therapy (all claimed).

ADVANTAGE - The selective cytokine inhibitory drug is useful in the treatment of various type of cancer and diseases associated with **angiogenesis** as well as to reduce or avoid the adverse side effects caused by the treatments such as radiation therapy and biological therapy.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B01-B02; B02-D; B02-T; B04-B03A; B04-B04D; B04-B04E; B04-F01; B04-H02B; B04-H04A; B04-H04C; B04-H07; B06-D03; B06-H; B07-H; B10-B01A; B10-C04A; B14-A01; B14-A01A2; B14-A02A3; B14-A03; B14-A04; B14-C03; B14-C09B; B14-D05C; B14-E08; B14-F02D; **B14-F02F1**; B14-F03; B14-G02; B14-G02A; B14-G02D; B14-H01; B14-J01B4; B14-J05B; B14-N03; B14-N17; B14-N17B; B14-N17D; B14-S04

M1 *17* DCN: RA09LI-K; RA09LI-T; RA09LI-M; RA0O3V-K; RA0O3V-T; RA0O3V-M

M1 *18* DCN: RA0DNM-K; RA0DNM-T; RA0DNM-M; RA0KDA-K; RA0KDA-T; RA0KDA-M

M1 *19* DCN: RA1WOE-K; RA1WOE-T; RA1WOE-M

M1 *20* DCN: RA04TA-K; RA04TA-T; RA04TA-M

M2 *01* DCN: RA4TIW-K; RA4TIW-T; RA4TIW-M; RA4TIW-U

M2 *02* DCN: **RACI5Z-K**; **RACI5Z-T**; **RACI5Z-M**; **RACI5Z-U**

M2 *03* DCN: 0115-62601-K; 0115-62601-T; 0115-62601-M; 0115-62601-U

M2 *04* DCN: 0115-62602-K; 0115-62602-T; 0115-62602-M; 0115-62602-U

M2 *05* DCN: R01166-K; R01166-T; R01166-M

M2 *06* DCN: RA035F-K; RA035F-T; RA035F-M; RA2PVY-K; RA2PVY-T; RA2PVY-M

M2 *07* DCN: R10440-K; R10440-T; R10440-M

M2 *08* DCN: RA01E9-K; RA01E9-T; RA01E9-M

M2 *09* DCN: R10124-K; R10124-T; R10124-M

M2 *10* DCN: R02028-K; R02028-T; R02028-M; R08024-K; R08024-T; R08024-M

M2 *11* DCN: R00125-K; R00125-T; R00125-M; R17770-K; R17770-T; R17770-M

M2 *12* DCN: R08225-K; R08225-T; R08225-M

M2 *13* DCN: RA021Q-K; RA021Q-T; RA021Q-M

M2 *14* DCN: R17804-K; R17804-T; R17804-M

M2 *15* DCN: R07202-K; R07202-T; R07202-M

M5 *16* DCN: R00002-K; R00002-T; R00002-M; R14648-K; R14648-T; R14648-M

DCRE 433262-0-0-0; 817201-0-0-0; 106545-2-0-0; 109181-1-0-0; 14620-0-0-0; 93613-1-0-0; 91082-0-0-0; 8769-1-0-0; 110156-1-0-0; 92243-0-0-0; 8220-2-0-0; 133806-1-0-0; 10897-0-0-0; 88752-2-0-0; 91489-0-0-0; 114126-0-0-0; 94348-0-0-0; 97947-0-0-0

ABEX UPTX: 20040112

SPECIFIC COMPOUNDS - The use of 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-

dihydro-isoindol-2-yl)-propionamide and cyclopropanecarboxylic acid (2-(1-(3-ethoxy-4-methoxy-phenyl)-2-methane sulfonyl-ethyl)-3-oxo-2,3-dihydro-1H-isoindol-4-yl-amide are specifically claimed as selective cytokine inhibitory drug.

ADMINISTRATION - 1-5000 mg of cytokine inhibitory drug is administered per day (claimed). The composition (I) is administered by oral, mucosal (e.g. nasal, sublingual, vaginal, buccal or rectal), parenteral (e.g. subcutaneous, intravenous, bolus injection, intramuscular or intraarterial), topical (e.g. eye drops or other ophthalmic preparations), transdermal or transcutaneous routes. The dosage amount of second active ingredient is 1-1000 mg (preferably 50-200 mg).

TECH UPTX: 20040112

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The cytokine inhibitory drug is a compound of formula (I) or (II).

In (I),

R5 = O-phenylene optionally substituted with T and M;

R7 = phenyl, benzyl (all optionally substituted with T or 1-10C alkoxy), benzyloxy or naphthyl;

R12 = OH, 1-12C alkoxy or N(R8R9);

R8 = H or 1-10C alkyl;

R9 = H, 1-10C alkyl, COR10 or SO2R10;

R10 = H, 1-10C alkyl or phenyl;

T = NO2, CN, CF3, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, OH, NH2, 1-10C alkyl or halo;

M = alkylamino, dialkylamino or acylamino; and

n = 0-3.

In (II),

R1, R2 = H or lower alkyl;

R1R2 + depicted carbon = O-phenylene, O-naphthylene or cyclohexane-1,2-diyl (optionally substituted with 1-4 groups of 1-10C alkoxy, T or M);

R3 = phenyl (optionally substituted with 1-4 groups of 1-10C alkoxy, T, M, 1-10C alkylthio, benzyloxy, 3-10C cycloalkoxy, 4-6C cycloalkylidene methyl, 3-10C alkylidenemethyl or indanyloxy);

R4 = H, 1-6C alkyl, phenyl or benzyl;

R4a = H or 1-6C alkyl;

R5a = CH2, CH2CO, SO2, S or NHCO; and

n' = 0-2.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The preferred compositions comprise the following:

(a) The treatment, management or prevention of a specific cancer (I) further comprises a second active ingredient, radiation therapy, hormonal therapy, biological therapy or immuno therapy;

(b) the treatment, management or prevention of a specific cancer further comprises a transplantation of umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow in the patient (all are processed umbilical cord blood, processed placental blood, processed peripheral blood stem cell, processed hematopoietic stem cell preparation or processed bone marrow).

Preferred Process: In the treatment, management or prevention of a specific cancer, a selective cytokine inhibitor drug is administered prior to, after, during the administration of a second active ingredient, biological therapy, radiation therapy, hormonal therapy, immuno therapy (transplantation of cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow in the patient) or surgery directed at relieving, reducing or avoiding a symptom of a specific cancer in the patient.

Preferred Components:

(a) The specific cancer is preferably refractory to conventional therapy;

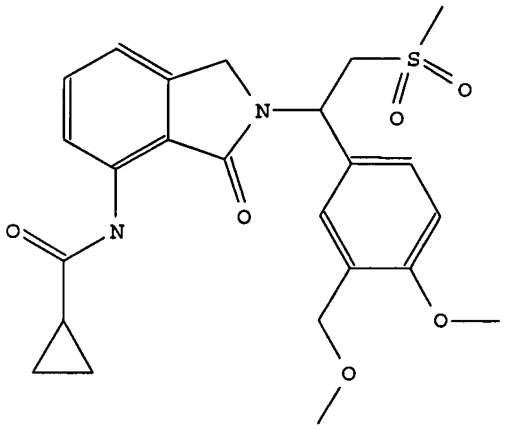
(b) The selective cytokine inhibitory drug used is enantiomerically pure; and

(c) The second active ingredient is hematopoietic growth factor, cytokine, anti-cancer agent, antibiotic, Cox-2 inhibitor, immunomodulatory agent, immunosuppressive agent, corticosteroid or a pharmacologically active mutant or their derivative (preferably oblimersen, melphalan, G-CSF,

GM-CSF, EPO, a Cox-2 inhibitor, topotecan, pentoxifylline, ciprofloxacin, taxotere, iritotecan, dexamethasone, doxorubicin, vincristine, IL 2, IFN, dacarbazine, Ara-C, vinorelbine, isotretinoin or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate or their prodrug or a pharmacologically active mutant or derivative).

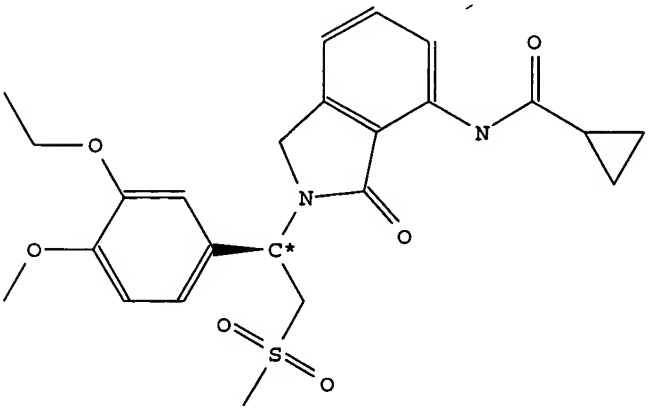
=> d ide l31 tot

L31 ANSWER 1 OF 4 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN.S **DCR-1178756**
DCSE 1178756-0-0-0
CN.S Cyclopropanecarboxylic acid {2-[2-methanesulfonyl-1-(4-methoxy-3-methoxymethyl-phenyl)-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide



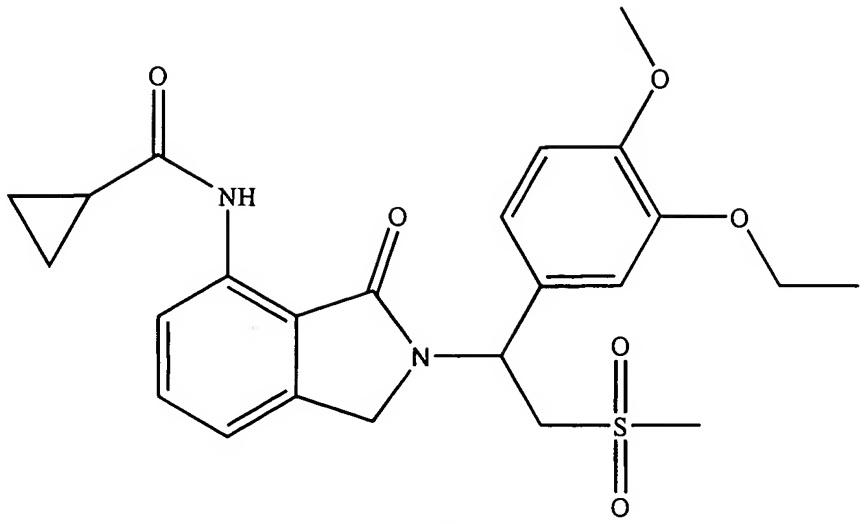
MF **C24 H28 N2 O6 S**

L31 ANSWER 2 OF 4 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN.S **DCR-956381**
DCSE 817201-2-0-0
CN.S Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide



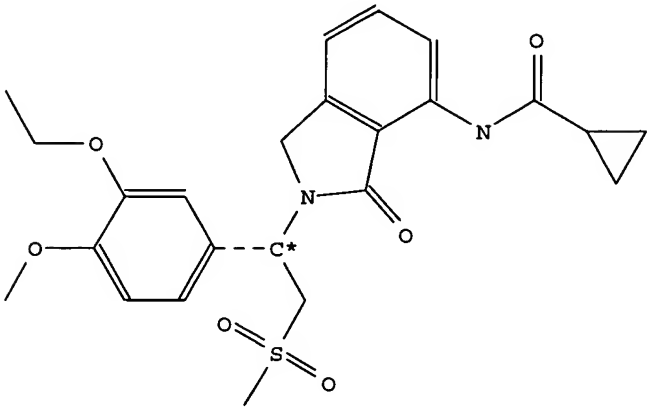
MF **C24 H28 N2 O6 S**

L31 ANSWER 3 OF 4 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN.S **DCR-956380**



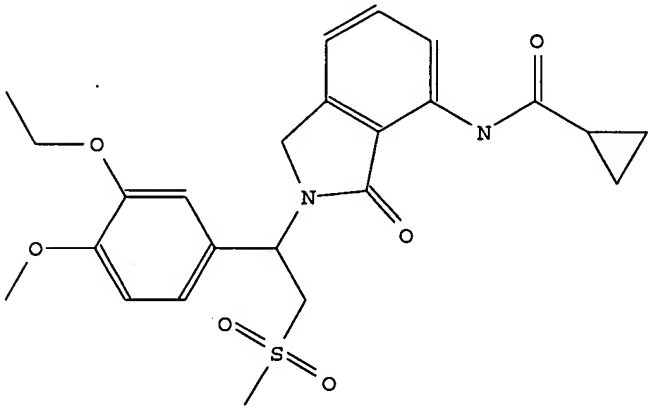

$C_{24}H_{28}N_2O_6S$

DCSE 817201-1-0-0
CN.S Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide



MF **C24 H28 N2 O6 S**

L31 ANSWER 4 OF 4 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN.S **DCR-817201**
DCSE 817201-0-0-0
CN.S Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide



MF **C24 H28 N2 O6 S**

=> d his

(FILE 'HOME' ENTERED AT 08:31:10 ON 20 JUL 2006)

FILE 'HCAPLUS' ENTERED AT 08:32:26 ON 20 JUL 2006
L1 1 US2006035955/PN OR (US2005-534325 OR WO2003-US35545)/AP,PRN
E ZELDIS J/AU
L2 93 E3-7
E CELGENE/CS,PA
L3 207 CELGENE/CS,PA
L4 18 CELGEN/CS,PA

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     FILE 'REGISTRY' ENTERED AT 08:34:19 ON 20 JUL 2006

     FILE 'HCAPLUS' ENTERED AT 08:34:26 ON 20 JUL 2006
L5             TRA L1 1- RN :       21 TERMS

     FILE 'REGISTRY' ENTERED AT 08:34:26 ON 20 JUL 2006
L6           21 SEA L5
L7            1 L6 AND C3/ES AND NC4-C6/ES AND 46.150.18/RID
L8          381 C24H28N2O6S
L9            3 L8 AND C3/ES AND NC4-C6/ES AND 46.150.18/RID
                SAV TEM GEM325C3/A L9

     FILE 'HCAPLUS' ENTERED AT 08:36:56 ON 20 JUL 2006
L10          18 L9
                E ANGIOGENESIS/CT
L11       19056 E3-8
                E E3+ALL
L12       19056 E7
                E ANGIOGENESIS INHIBITORS/CT
                E E3+ALL
L13        7571 E4
                E E10
L14        2169 E3-6
                E E3+ALL
L15       17954 E7+OLD,NT
L16          17 L10 AND L1-4
L17           5 L10,L16 AND L11-15

     FILE 'HCAOLD' ENTERED AT 08:44:54 ON 20 JUL 2006
L18           0 L9

     FILE 'USPATFULL, USPAT2' ENTERED AT 08:45:01 ON 20 JUL 2006
L19          13 L9
                E ANGIOGENESIS/CT
L20        5261 E3-4
L21         790 E5
L22           2 L19 AND L20-21

     FILE 'USPATFULL, USPAT2' ENTERED AT 08:45:58 ON 20 JUL 2006

     FILE 'MEDLINE' ENTERED AT 08:46:13 ON 20 JUL 2006
L23           0 L9

     FILE 'EMBASE' ENTERED AT 08:46:23 ON 20 JUL 2006
L24           0 L9

     FILE 'BIOSIS' ENTERED AT 08:46:29 ON 20 JUL 2006
L25           0 L9

     FILE 'WPIX' ENTERED AT 08:47:02 ON 20 JUL 2006
L26           1 L1
                SEL DCRE
                EDIT /DCRE /DCSE
L27          21 E1-21
L28           1 DCR-817201/AN.S
L29          12 C24 H28 N2 O6 S/MF
L30           4 L29 AND (DCR-1178756 OR DCR-956381 OR DCR-956380 OR DCR-817201)
L31           4 L28,L30
                SEL DCSE L31
                EDIT /DCSE /DCRE
L32          10 E22-25
                SEL SDCN L31
                EDIT /SDCN /DCN
L33          10 E26-29
L34          10 L32-33
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L35          10 L31/DCR
L36          10 L34-35
L37           3 L36 AND ?ANGIOGEN?
L38           3 L36 AND (B14-F02F? OR C14-F02F?)/MC
L39           5 L36 AND P52?/M0,M1,M2,M3,M4,M5,M6
L40       21259 A61P009/IPC,IC,ICM,ICS,ICA,ICI
L41           2 L36 AND L40
L42           5 L37-39,L41

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